

Text and Atlas of Wound Diagnosis and Treatment, 2e >

Chapter 8: Atypical Wounds

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INTRODUCTION

CHAPTER OBJECTIVES

At the end of this chapter, the learner will be able to:

1. Recognize signs of an atypical wound.
2. Categorize an atypical wound according to a basic pathology.
3. Determine the appropriate medical specialist for a given wound.
4. Develop an evidence-based care plan for an atypical wound.
5. Educate the patient and family about the wound diagnosis.

Most wounds are diagnosed as arterial, venous, pressure, neuropathic, surgical, or burn and are treated according to the principles that have been discussed in the previous chapters. If a wound has a different appearance or does not respond to standard care, the clinician is challenged to determine either the factors that are inhibiting healing *or* to consider a different diagnosis. This chapter reviews the basic morphology of skin disease, red flags of atypical wounds, and characteristics of different diagnostic categories. The pathophysiology, clinical presentation with photographs, differential diagnosis, medical management, and wound management of each wound category are provided to assist the clinician in making sound clinical decisions.

CHARACTERISTICS OF ATYPICAL WOUNDS

The first indication that a wound is atypical is that little signal in the clinician's instinct that says, "This is just not quite what it looks to be." And usually it behooves the clinician to follow those instincts, to at least rule out an atypical diagnosis, and at most to make a differential diagnosis that completely changes the care plan and results in wound healing. **TABLE 8-1** provides a list of characteristics that suggest a wound does not fall into the typical categories.^{1,2}

TABLE 8-1

Characteristics of Atypical Wounds

- Unusual location
- Unusual age of patient
- Asymmetric lesion
- Granulation extending over the wound edge
- Exuberant granulation tissue or callus
- Friable granulation tissue
- Purple-red color around ulcer (termed *violaceous*)
- Ulcer in center of pigmented lesion
- History of repeated trauma
- Rolled out edges
- Fungating growth
- History of radiation therapy
- Wound secondary to burns, trauma, and diabetes
- No obvious diagnosis

MORPHOLOGY OF SKIN DISEASE

Many diseases will cause changes in the skin that are predictable and/or suggestive of a certain diagnosis. **TABLE 8-2** provides a list of terms and definitions of integumentary characteristics (based on size, texture, and color) that are used to describe abnormal skin appearance.² These terms are used in the following descriptions of atypical wound clinical presentations.

TABLE 8-2

Skin Disease Morphology

1. Macule—A circumscribed, flat, nonpalpable lesion that is flush with the level of surrounding normal skin; smaller than 10 mm in diameter
2. Patch—A flat, nonpalpable lesion that is flush with the level of surrounding normal skin; greater than 10 mm in diameter
3. Papule—A superficial, circumscribed dome-shaped or flat topped palpable lesion elevated above the skin surface; less than 10 mm in diameter
4. Plaque—A lesion that rises slightly above the surface of the skin; greater than 10 mm in diameter
5. Nodule—A firm lesion that is thicker or deeper than the average plaque or papule; is palpable as differentiated tissue
6. Vesicle—An elevated lesion that contains clear fluid; less than 10 mm in diameter
7. Bulla—An elevated lesion that contains clear fluid; greater than 10 mm in diameter
8. Pustule—An elevated lesion that contains pus
9. Urticarial (hives)—An allergic reaction characterized by white fluid-filled blisters (termed wheals) surrounded by erythema (flares)
10. Livedo reticularis—A mottled, lace-like purplish discoloration of the skin caused by thrombotic occlusion of the capillaries that leads to swelling of the venules

CATEGORIES OF ATYPICAL WOUNDS

The atypical wounds discussed in this chapter can be categorized into the following groups: allergic reactions, autoimmune disorders, Herpes virus, infected wounds (bacterial and fungal), malignant wounds, and miscellaneous. Some categories will have common signs and symptoms and yet

discrete but definite differences, and similar treatment strategies. The list is by no means exhaustive— that would be beyond the scope of this chapter!

ALLERGIC REACTIONS

Allergic reactions can be either contact (the offending substance touches the skin) or systemic (the offending substance is injected or ingested). In either case, the substance, termed an antigen, causes an immunological response that results in the production of antibodies and a subsequent inflammatory response. The reaction can actually cause wounds to develop, or in the case of existing wounds, prevent healing from progressing.

Contact Dermatitis

Pathophysiology

Contact dermatitis can be either *allergic* or *irritant*, depending on the host immune system and the concentration of the irritant.³ In *allergic contact dermatitis*, the offending substance or contact allergen (ie, a nonprotein chemical called hapten) reacts with the skin barrier to activate the innate immune response. The allergen binds to the carrier protein and creates a sensitizing antigen, the Langerhans cells carry the antigen to the T cells (specifically CD8⁺ T cells that are primed in lymphoid organs during sensitization and recruited in the skin upon re-exposure to the hapten),⁴ and the T cells cause the release of lymphokines.⁵ Thus develops the inflammatory symptoms of erythema, rash, itching, and in some cases vesicular lesions, followed by scaling and dry skin (FIGURES 8-1 and 8-2).⁴ The allergic response can be either immediate or delayed, and can involve both the skin and the subcutaneous tissue. Usually the response increases in severity after repeated exposures; sensitization upon first exposure may last 10–15 days with no clinical consequence and upon re-exposure clinical symptoms may appear within 24–72 hours.⁴

FIGURE 8-1

Contact dermatitis Characteristics of contact dermatitis seen on the lower extremity are a well-defined border of exposure, erythema, rash (at the proximal aspect of the wound), and patient complaint of itching under the bandages. Some of the dressing components that can cause an allergic reaction are sulfa, [silver](#), silicone, [iodine](#), or latex. Careful subjective history about possible allergies is important to minimize the risk of reactions that may inhibit wound healing or even extend the wound.



Source: Rose L. Hamm: *Text and Atlas of Wound Diagnosis and Treatment*, 2e
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FIGURE 8-2

Contact dermatitis This patient with a known latex allergy was being treated for a chronic venous wound using antimicrobial dressings and multilayered compression bandages. After progressing well for several months, the wound and periwound tissue began to deteriorate with numerous areas of partial thickness skin loss like the one proximal to the primary wound. Cessation of any dressings that contained [silver](#) resulted in an immediate reversal of the symptoms, confirming a suspicion that she had a [silver](#) allergy. Both infection and an allergic reaction can cause

deterioration of the wound bed, and are obviously treated quite differently. Confirmation of infection is by culture; and of allergy, by removing the suspected offending agent.



Source: Rose L. Hamm: *Text and Atlas of Wound Diagnosis and Treatment*, 2e
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The *irritant type of contact dermatitis* is not an immunological response but a reaction to a caustic substance and depends on the concentration of the substance, for example, a chemical or topical liquid. Some antiseptics, eg, acetic acid or Dakin's solution, may cause irritant contact dermatitis if used repeatedly or in strong concentrations.

Patients with chronic leg wounds have an increased susceptibility to allergic contact dermatitis,⁶ especially if they are being treated with compression therapy, a condition sometimes referred to as *stasis dermatitis*. If contact dermatitis is suspected or if the patient reports a history of allergies to other substances, patch testing can be performed to confirm the diagnosis.⁷ **TABLE 8-3** provides a list of common allergens for patients who have wounds.

TABLE 8-3

Common Allergens for Contact Dermatitis

Contact allergens

Neomycin
Bacitracin
Wool
Alcohol
Formaldehyde
Parabens
Tape adhesives
Latex
Perfumes
Metals (eg, nickel, silver)

Irritant allergens

Soap
Detergent
Cleaning solvents
Poison ivy or oak
Pesticides

Clinical Presentation

Signs of dermatitis include erythema, weeping, scaling of the periwound area, and itching. It can occur at any age; however, in the older population it can easily be misdiagnosed. In severe cases, shiny skin and alopecia may develop. A visible determining factor is that the symptoms occur only in areas of direct contact with the irritating material.

Differential Diagnosis

- Cellulitis
- Vasculitis
- Atopic dermatitis (chronic dermatitis associated with asthma and inhalant allergies; hereditary)
- Nummular dermatitis (distinct round or oval patches that begin as blisters, often after skin injury; a result of sensitivity to applied topical ointments or metals)

Medical Management

The most important component of treating any dermatitis is the identification and discontinuation of the medication, dressing, or other substance that might be responsible for contact dermatitis. In the acute phase, low-dose topical steroids and antihistamines may help decrease inflammation and discomfort; systemic steroids may be beneficial if there is an extensive area of contact dermatitis. Antibiotics are indicated only if there is evidence of secondary infection.⁵

Wound Management

Patients usually require only supportive care and discontinuation of the irritating topical agent and, in the case of an existing wound, substitution of a dressing that has fewer or no allergens. Nonadherent hypoallergenic dressings are recommended for care of open lesions. Most products that are used for wound care are available in latex-free forms, as both patients and clinicians can suffer from latex allergies. The skin will usually heal in 2 to 3 weeks.

Drug-Induced Hypersensitivity Syndrome

Pathophysiology

Drug-induced hypersensitivity syndrome (DIHS) is an immunologic response to a drug received either orally, by injection, or by IV. Although not fully understood, the process is similar to what occurs with skin allergies except that the immune response is activated by the causative agents and their metabolites rather than by a direct effect on the keratinocytes.⁸ There are numerous syndromes based on severity, types of lesions, and underlying diseases processes; however, all of them produce generalized (rather than localized) skin lesions and systemic symptoms (**TABLE 8-4**).

TABLE 8-4

Drug-Induced Hypersensitivity Syndrome

| Syndrome | Description |
|--|---|
| Erythema multiforme | Generalized rash with macular or popular skin eruptions; affects 20- to 40-year-olds |
| Drug rash with eosinophilia and systemic systems (DRESS Syndrome) | Three of the following symptoms are necessary for diagnosis: fever, exanthema, eosinophilia, atypical circulating lymphocytes, lymphadenopathy, hepatitis |
| Stevens–Johnson syndrome | Cutaneous lesions of papules, vesicles, or bullae covering <10% of the body surface area; mucosal lesions; conjunctivitis |
| Toxic epidermal necrolysis | Cutaneous lesions of papules, vesicles, or bullae covering >30% of the body surface area; mucosal lesions; conjunctivitis |
| Chemotherapy-induced acral erythema | Painful swelling and erythema of the palms and soles of patients on high-dose chemotherapy |
| Drug-induced lupus erythematosus | Lupus-type symptoms with skin signs associated with medications; resolves when medications withdrawn |

Some of the more common drug-hypersensitivity syndrome nomenclature and symptoms that have been reported in the literature.

From Hamm RL. Drug-induced hypersensitivity syndrome: diagnosis and treatment. *J Am Coll Clin Wound Spec.* 2012;3(4):77–81.

Adverse drug reactions have been classified as Type A: those that are predictable and dose-dependent reactions, including overdose, side effects, and drug interactions (eg, a gastrointestinal bleed following treatment with non-steroidal anti-inflammatory drugs [NSAIDs]); and Type B, those that are unpredictable, more likely to be dose independent, and may include immunologically mediated drug hypersensitivity or non-immune-mediated reactions, thus being considered allergic reactions.⁹ The most commonly reported medications that cause DIHS are listed in **TABLE 8-5**.

TABLE 8-5

Most Commonly Reported Medications That Cause Drug-Induced Hypersensitivity Reactions

| Drug Class | Specific Drug | Latent Period |
|------------|---------------|---------------|
|------------|---------------|---------------|

| | | |
|--|--|---|
| Angiotensin-converting enzyme inhibitors | Captopril | At any time |
| Xanthine oxidase inhibitor | Allopurinol | 2–6 weeks ¹⁰ |
| Antibiotics | Beta-lactams (pediatrics) ¹¹ | Immediate: 1 hourNon-immediate: ≥1 hour ¹² |
| | Ceftriaxone | 72 hours ¹³ |
| | Cyclosporine | |
| | Dapsone | Few days to weeks ¹⁴ |
| | Isoniazid | |
| | Levofloxacin | |
| | Minocycline | |
| | Penicillin | |
| | Sulfonamides | |
| | Trimethoprim | |
| Anticonvulsants | Carbamazepine | Usually 2–4 weeks; can be up to 3 months |
| | Lamotrigine | |
| | Phenobarbitone | |
| | Phenytoin | |
| | Primidone | |
| Antidepressants | Clomipramine (anafranil) | |
| Antifungals | Terbinafine | 2–3 days |
| Antiretrovirals | Abacavir | |
| | Nevirapine | |
| Beta-blocker | Atenolol | |
| Biologic modifiers | Infliximab | |
| | Murine and humanized monoclonal antibodies | |
| | Recombinant interferons | |
| Drug coloring agents | Blue dyes | |

| | | |
|--|--------------------------|----------|
| Calcium channel blockers | Diltiazem | 2–3 days |
| Gold salts | | |
| Antihypertensive | Hydralazine (apresoline) | |
| Immunosuppressants | Azathioprine | |
| Non-steroidal anti-inflammatory drugs | Aspirin | |
| Antiarrhythmic | Procainamide | |
| Sodium channel blockers | Mexiletine | |
| Disease-modifying anti-rheumatic drugs | Sulfasalazine | |

Used with permission from Hamm, RL. Drug allergy: delayed cutaneous hypersensitivity reactions to drugs. *EMJ Allergy Immunol.* 2016;1(1):92–101. Available at: <https://www.emjreviews.com/allergy-immunology/article/drug-allergy-delayed-cutaneous-hypersensitivity-reactions-to-drugs>. Accessed July 25, 2018.

Clinical Presentation

Symptoms include generalized rash (with or without vesicles) and any of the following: local eruptions, fever, lymphedema, mucosal lesions, conjunctivitis, and epidermal sloughing (**FIGURE 8-3**). Onset is usually 1–3 weeks after the first exposure to the offending drug, beginning with a fever or sore throat and progressing to the cutaneous/mucosal involvement. In the younger adult population (20–40 years), the syndrome is termed *erythema multiforme*.

FIGURE 8-3

Drug-induced hypersensitivity syndrome Diffuse generalized rash (with or without vesicles)—with symptoms of local eruptions, fever, lymphedema, mucosal lesions, conjunctivitis, and epidermal sloughing—can occur on any part of the body as a result of an allergic or hypersensitive reaction to ingested medications. Unlike a localized contact allergic response, DIHS involves a larger surface area without direct exposure to a specific substance.



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Differential Diagnosis

- Infection
- Vasculitis
- Contact dermatitis

Medical Management

Medical management begins with identification and cessation of the causative agent, which is usually the last one that the patient has initiated taking. Depending on the severity of the symptoms, corticosteroids are used to prevent progression and relieve symptoms, and supportive care is provided in an intensive care unit or a burn unit for more severe cases.

Wound Management

In minor cases, cessation of the medication may be sufficient to reverse symptoms and no wound care is needed. In more severe cases with epidermal sloughing, treatment is similar to that of a deep superficial burn except that debridement of the detached epidermal tissue is usually not advisable because of potential loss of fluids. Nonadherent antimicrobial dressings are recommended to help prevent infection and to avoid further skin tearing with dressing changes. Prevention of fluid loss and infection are paramount, and as the patient improves, dressings to promote re-epithelialization are advised.

AUTOIMMUNE DISORDERS

Scleroderma

Pathophysiology

Scleroderma (systemic sclerosis) is a chronic autoimmune disease of unknown etiology that usually affects women between the ages of 30 and 50 and results in extensive scarring and disfigurement as it progresses.¹⁵ The skin becomes thick and hard (sclerotic) with a buildup of scar tissue, resulting in loss of skin elasticity, joint range of motion, muscle strength, mobility, and function. There is also damage to internal organs such as the heart and blood vessels, lungs, esophagus, kidneys, and other organs, which is a major factor in determining prognosis for each individual patient.¹⁶

Recent studies suggest both a genetic susceptibility and a predisposition to scleroderma. The most robust associations include genes for B- and T-cell activation and innate immunity; other pathways include genes involved in extracellular matrix deposition, cytokines, and autophagy (the natural, regulated mechanism of cellular activity that allows orderly degradation and recycling of cellular components).¹⁷ The sequence of scleroderma involves the following: arteriole endothelial cells die by apoptosis and are replaced by collagen; inflammatory cells infiltrate the arteriole and cause more damage, resulting in the scarred fibrotic tissue that is the hallmark of scleroderma.^{18,19}

Clinical Presentation

The two main types of scleroderma are *localized* and *systemic*. Localized is further differentiated into *morphea* with discolored patches on the skin, and *linear* with streaks or bands of thick hard skin on the arms and legs. Localized scleroderma only affects the skin and not the internal organs. Systemic scleroderma can be limited (affecting only the arms, hands, and face) or diffuse (rapidly progressing, affecting large areas of the skin and one or more organs). Thirty-five percent of the patients with scleroderma develop skin ulcers that are painful, refractory, and usually over bony prominences (FIGURE 8-4). CREST, a limited systemic form of scleroderma, is described in TABLE 8-6; however, it does not reflect the internal organ involvement that may also be present. In addition, patients may experience joint pain, fatigue, depression, reduced libido, and altered body image. A third type is limited systemic sclerosis, also known as *sine scleroderma*, which includes Raynaud's phenomenon and internal involvement without sclerotic skin.²⁰

FIGURE 8-4

Scleroderma Scleroderma causes the skin to lose its elasticity, resulting in loss of joint range of motion, strength, and function. The thick linear bands around the fingers are indicative of localized linear scleroderma.



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TABLE 8-6

Symptoms of CREST, a Scleroderma Syndrome

- Calcinosis—calcium deposits, usually in the fingers
- Raynaud phenomenon—color changes in fingers and sometimes toes after exposure to cold temperatures
- Esophageal dysfunction—loss of muscle control, which can cause difficulty swallowing
- Sclerodactyly—tapering deformity of the bones of the fingers
- Telangiectasia—small red spots on the skin of the fingers, face, or inside of the mouth

Differential Diagnosis

Other systemic autoimmune diseases, for example, systemic lupus erythematosus and rheumatoid arthritis.

Medical Management

Because the etiology is unknown, treatment of scleroderma centers on alleviating symptoms, preserving skin integrity with protective strategies, preventing infection, and controlling inflammation to minimize severity.²¹ d-penicillamine, colchicine, PUVA, relaxin, cyclosporine, and omega-oil derivatives have been used to treat the skin fibrosis. Immunosuppressive agents such as methotrexate and cyclosporine have been used to treat the systemic disease, and plasmapheresis can be used in severe cases.^{1,22}

Wound Management

Local wound care is tedious because of the high pain levels associated with open wounds on sclerotic skin, and wound healing is impeded by the scarring of the subcutaneous tissue and the immunosuppressive medications. Enzymatic debridement with collagenase may be helpful with painful wounds, as well as occlusive dressings to help with autolytic debridement. Nonadherent dressings are advised both to minimize pain and avoid tearing skin upon removal. Silicone-backed foam dressings are useful as secondary dressings. Patient education regarding protective measures for skin is crucial, for example, using gloves when doing housework, avoiding caustic liquids, wearing warm clothes to avoid Raynaud's phenomenon, and using moisturizers to avoid dry skin. As the disease progresses, custom shoes with molded inserts to accommodate changes in the shape of the feet can help maintain independent ambulation.

Vasculitis

Pathophysiology

Vasculitis is an inflammatory disorder of blood vessels, which can ultimately result in organ damage, including the skin. The etiology is often idiopathic—it is a reaction pattern that may be triggered by certain comorbidities including underlying infection, malignancy, medication, and connective tissue diseases such as systemic lupus erythematosus (FIGURE 8-5). Circulating immune complexes (antibody/antigen) deposit in the blood vessel walls, causing inflammation that may be segmental or involve the entire vessel. At the site of inflammation, varying degrees of cellular inflammation and resulting necrosis or scarring occur in one or more layers of the vessel wall, and inflammation in the media of the muscular artery tends to destroy the internal elastic lamina.^{23,24}

FIGURE 8-5

Vasculitis due to SLE Vasculitis presents as dermal necrosis as a result of occluded small arterioles and is exquisitely painful, making local care very difficult. Patients with autoimmune disorders, for example, systemic lupus erythematosus (SLE), are at greater risk for vasculitis. The medications used to treat SLE further complicate and inhibit wound healing; however, the first medical priority is to suppress the inflammatory response.



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Leukocytoclastic vasculitis, a histopathologic term used to describe findings in small-vessel vasculitis, refers to the breakdown of inflammatory cells that leaves small nuclear fragments in and around the vessels. Vasculitic inflammation tends to be transmural, rarely necrotizing, and nongranulomatous. Resolution of the inflammation tends to result in fibrosis and intimal hypertrophy, which in combination with secondary clot formation can narrow the arterial lumen and account for the ischemia or necrosis of the tissue supplied by the affected vessels.²⁵ Clinical symptoms (ie, tissue loss) depend on the artery or arteries that are involved and the extent of lumen occlusion. Cutaneous vasculitis usually occurs in the lower extremities and feet. Vasculitic syndromes based on the affected vessels are listed in **TABLE 8-7**.

TABLE 8-7

Vasculitic Syndromes Based on Affected Vessels

| Name | Typical Vessels Involved | Symptoms |
|--|-------------------------------|--|
| Behçet's disease | Small vessels | Recurrent painful lesions in the mouth, on the genitals, on the skin (acne-like), or in the eye (uveitis); limb claudication |
| Buerger's disease (thromboangiitis) | Vessels to the hands and feet | Typically in smokers; thin shiny skin, thick nails, pain in hands and/or feet; cyanosis that may result in tissue necrosis |
| Churg–Strauss syndrome (eosinophilic granulomatosis with polyangiitis) | Small and medium vessel | Three stages: 1. Airway inflammation, asthma, allergic rhinitis 2. Hypereosinophilia 3. Vasculitis with tissue necrosis, beginning with purpura |
| Cryoglobulinemia | Small vessels | Often associated with hepatitis C; appears as painful purpura that progresses to full-thickness, often infected wounds; usually on this distal digits. Precipitated by exposure to cold environment that leads to presence of coagulated cryoglobulins that clog the small vessels |
| Giant cell arteritis | Temporal and cranial arteries | Headaches, temporal pain, visual disturbances, scalp sensitivity, dry cough with respiratory symptoms, fever, upper extremity weakness and sensory changes, unequal BP measurements or unequal/absent pulses in the limbs. May be associated with polymyalgia rheumatica |

| | | |
|---|---|---|
| Henoch–Schönlein purpura (IgA vasculitis) | Small vessels | Purpura, arthritis, abdominal pain (usually in children) |
| Hypersensitivity vasculitis (allergic vasculitis, cutaneous vasculitis, or leukocytoclastic vasculitis) | Small vessels to the skin | Purpura, usually on the lower extremities or back (in bedridden patients) due to an allergic reaction to a medication |
| Immune complex–associated vasculitis | Small vessels to neurons | Peripheral neuropathy |
| Kawasaki's disease | Any of the vessels, any size | Skin erythema, enlarged lymph nodes, red mucous membranes, and in some cases heart problems; occurs in childhood |
| Microscopic polyangiitis | Small vessels to organs | Ischemia, hemorrhage, loss of organ function |
| Polyarteritis nodosa | Small and medium arteries | Subcutaneous nodules or projections of lesions; fever, chills, tachycardia, arthralgia, myositis, motor and sensory neuropathies |
| Primary angiitis of the CNS | Small and medium vessels in the brain and spinal cord | Brain: headache, altered mental status, focal CNS deficits; spinal cord: lower extremity weakness, bladder dysfunction |
| Takayasu's arteritis | Aorta, aorta branches, pulmonary arteries | Inflammatory phase with flu-like symptoms, pulseless upper extremity, claudication, renal artery disease; fatigue, night sweats, sore joints, and weight loss may occur first |
| Wegener's granulomatosis (granulomatosis with polyangiitis) | Small and medium vessels | Organ failure (lung and kidneys), variable including skin, depending on the vessels involved |

Note: The trend is to classify the diseases by descriptive names rather than by names referring to the discovering physician.

Adapted from Hamm R. Why isn't this wound healing? In Schiffman M, ed. *Recent Clinical Techniques, Results, and Research in Wounds*. Springer; 2018. doi: 10.1007/15695_2017_105.

<https://www.nhlbi.nih.gov/health/health-topics/topics/vas/types>.

<http://www.merckmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/vasculitis>.

Clinical Presentation

Clinical presentation of cutaneous vasculitis, which varies depending on the arterial involvement, includes palpable purpura, livedo reticularis, pain, skin lesions with or without nodules, and tissue necrosis. It may present as one large necrotic lesion or several small lesions, but all are full thickness after debridement. Systemic symptoms may also be present and usually relate to kidney, lung, or gastrointestinal tract involvement. On some occasions, signs of vasculitis in other organs may appear at the same time that skin lesions appear (**FIGURES 8-6 and 8-7**). One very distinctive characteristic for differential diagnosis from chronic venous wounds is the exquisite pain that occurs with vasculitis, making the initial local treatment

very tedious.

FIGURE 8-6

Vasculitis associated with other symptoms This patient with vasculitis of the posterior calf noted the onset of pain and dermal symptoms at the same time that he experienced neurological signs associated with what was diagnosed as a CVA. Both maladies occurred after the stress of losing a family member. Note the discoloration of the proximal periwound skin, indicating that the inflammation is still evolving.



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FIGURE 8-7

Vasculitis in the remodeling phase of healing The patient in [FIGURE 8-6](#) was treated with low-frequency noncontact ultrasound, nonadherent dressings to facilitate autolytic debridement, and compression therapy. He progressed to full closure of the wounds without surgical intervention. Topical 2% [lidocaine](#) gel was applied prior to each treatment to assist with pain management.



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Differential Diagnosis

- Giant cell arteritis
- Primary angiitis of the CNS
- Takayasu arteritis
- Churg–Strauss syndrome
- Immune complex–associated vasculitis
- Microscopic polyangiitis
- Polyarteritis nodosa
- Rheumatoid arthritis
- Wegener granulomatosis
- Henoch–Schönlein purpura
- Chronic venous insufficiency wounds

Medical Management

Treatment of any vasculitis depends on the etiology, extent, and severity of the disease. Ultrasound can be used to detect abnormalities in medium- and large-vessel disease, and to determine distribution or organ involvement in small vessel vasculitides.²⁶ For secondary vasculitic disorders, treating the underlying comorbidity (eg, infection, drug use, cancer, or autoimmune disorder) is crucial.

Remission of life- or organ-threatening disorders is induced by using cytotoxic immunosuppressants (e.g., [cyclophosphamide](#)) and high-dose corticosteroids, usually for 3–6 months, until remission occurs or until the disease activity is acceptably reduced. Adjusted treatment to maintain remission takes longer, usually 1–2 years. During this period, the goal is to eliminate corticosteroids, reduce the dosage, or use less potent immunosuppressants as long as needed. After tapering or eliminating corticosteroids, [methotrexate](#) or [azathioprine](#) can be substituted to maintain remission.²⁷

Wound Management

Initial treatment of wounds caused by vasculitis is extremely difficult because of the pain. The principles of standard wound care (debride necrotic tissue, treat inflammation and infection, apply moist wound dressings, nurture the edges, and ensure optimal [oxygen](#) supply, termed TIMEO₂)²⁸ are recommended. Topical [lidocaine](#) helps reduce pain during treatments, noncontact low-frequency ultrasound helps mobilize cellular activity and interstitial fluids, and compression therapy helps manage the edema that occurs in the lower extremities as a result of the inflammation and decreased mobility. Nonadherent dressings that promote autolysis of the necrotic tissue (eg, X-Cell, Medline, Mundelein, IL) are excellent initially, especially in reducing pain levels with dressing changes. Silicone-backed foam dressings are helpful in absorbing exudate as well as in reducing pain. If the patient is on steroids, local vitamin A can be used to negate the effects of steroids. As the acute inflammation recedes, pain levels decrease, and wound healing progresses to proliferation, treatment can be more aggressive with the goals of full re-epithelialization and return to prior level of function.

Antiphospholipid Syndrome

Pathophysiology

The antiphospholipid syndrome (APS) is an acquired autoimmune disorder in which antibodies are directed against one or more phospholipid-binding proteins (eg, anti- β 2-glycoprotein I, anticardiolipin, and lupus anticoagulant) or their associated plasma proteins, resulting in hypercoagulation within the microvasculature. APS is characterized by elevated titers of different antiphospholipid antibodies.¹⁸ The proteins normally bind to phospholipid membrane constituents and protect them from excessive coagulation activation. The autoantibodies displace the

protective proteins and thus produce procoagulant endothelial cell surfaces and cause arterial or venous thrombosis. In vitro clotting tests may paradoxically be prolonged because the antiprotein/phospholipid antibodies interfere with coagulation factor assembly and with activation on the phospholipid components that are added to plasma to initiate the tests.

The lupus anticoagulant is an antiphospholipid autoantibody that binds to protein-phospholipid complexes. It was initially recognized in patients with SLE; however, these patients now account for a minority of patients with the autoantibody. The lupus anticoagulant is suspected if the PTT is prolonged and does not correct immediately upon 1:1 mixing with normal plasma but does return to normal upon the addition of an excessive quantity of phospholipids (done by the hematology laboratory). Antiphospholipid antibodies in the patient plasma are measured by immunoassays of IgG and IgM antibodies that bind to phospholipid- β 2-glycoprotein I complexes on microtiter plates.¹⁸ APS can occur with or without associated rheumatic disease (eg, systemic lupus erythematosus).²⁹

Clinical Presentation

The arteriole thrombosis results in venous swelling, creating the typical livedo reticularis skin appearance. In addition, the lower extremities may have purpura, splinter hemorrhages, or superficial thrombophlebitis (**FIGURE 8-8**). As the disease progresses, skin necrosis may occur, and if the disorder occurs during pregnancy, there will be fetal demise. If the thrombosis is in the venules, the result may be DVT with lower extremity edema, tachypnea due to pulmonary emboli, and ascites.

FIGURE 8-8

Antiphospholipid syndrome Antiphospholipid syndrome is characterized in the early stages by livedo reticularis (resulting in small brown spots on the skin) and in the later stages by ischemic skin changes. (Used with permission from External Manifestations. In: Lichtman MA, Shafer MS, Felgar RE, Wang N, eds. *Lichtman's Atlas of Hematology 2016* New York, NY: McGraw-Hill; 2016. Available at:

<http://accessmedicine.mhmedical.com.ezproxy.cihe.edu.hk/content.aspx?bookid=1630§ionid=116918910>. Accessed August 02, 2018.)



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Differential Diagnosis

- Disseminated intravascular coagulation
- Infective endocarditis
- Thrombotic thrombocytopenic purpura

Medical Management

Asymptomatic individuals in whom blood test findings are positive do not require specific treatment.

Prophylactic therapy involves elimination of other risk factors such as oral contraceptives, smoking, hypertension, or hyperlipidemia. For patients with SLE, [hydroxychloroquine](#), an anti-inflammatory that may have intrinsic antithrombotic properties, may be useful. Statins are beneficial for patients with hyperlipidemia. If the patient has a thrombosis, full anticoagulation with intravenous or subcutaneous [heparin](#) followed by [warfarin](#) therapy is recommended.^{18,19,30}

Based on the most recent evidence, a reasonable target for the international normalized ratio (INR) is 2.0–3.0 for venous thrombosis and 3.0 for arterial thrombosis. Patients with recurrent thrombotic events, while well maintained on the above regimens, may require an INR of 3.0–4.0. For severe or refractory cases, a combination of [warfarin](#) and [aspirin](#) may be used. Treatment for significant thrombotic events in patients with APS is generally lifelong. Because cutaneous manifestations are the first sign of APS in up to 41% of patients, a full medical examination is advised for any patient showing the clinical symptoms in order to identify and treat the underlying pathology.^{31,32}

Wound Management

Conservative wound care is recommended for patients with skin lesions, keeping the wound moist and following wound bed preparation principles. Healing of wounds caused by other etiologies, eg, trauma or spider bites, will be delayed in patients who have APS.

Pemphigus

Pathophysiology

Pemphigus is an autoimmune blistering disease resulting from loss of normal intercellular attachments in the skin and oral mucosal membrane. Circulating antibodies attack the cell surface adhesion molecule desmoglein at the desmosomal cell junction in the suprabasal layer of the epidermis, resulting in the destruction of the adhesion molecules (acantholysis) and initiating an inflammatory response that causes blistering. There are three major forms of pemphigus: pemphigus foliaceus ([FIGURE 8-9](#)) and pemphigus vulgaris that have IgG autoantibodies against desmoglein 1 and desmoglein 3, respectively; and paraneoplastic pemphigus that has IgG autoantibodies against plakins and desmogleins ([FIGURE 8-10](#)).^{33,34}

FIGURE 8-9

Pemphigus Pemphigus foliaceus is characterized by blistering of the epidermis followed by crusting and sloughing, resulting in painful wounds and discoloration after healing. Complications include bacterial and viral infections as a result of the open wounds and immunosuppression, as well as sequelae from long-term use of corticosteroids (osteoporosis, avascular necrosis).



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FIGURE 8-10

Paraneoplastic pemphigus Characteristics of paraneoplastic pemphigus include extensive lesions on the lips, severe stomatitis, and erythematous macules and papules that coalesce into large cutaneous lesions. The lesions are diagnosed by biopsy that shows a mix of individual cell necrosis, interface change, and acantholysis. (Used with permission from Anhalt GJ, Mimouni D. Paraneoplastic pemphigus. In: Goldsmith LA, Katz SI, Gilchrist BA, Paller AS, Leffell DJ, Wolff K. eds. *Fitzpatrick's Dermatology in General Medicine*. 8th ed. New York, NY: McGraw-Hill; 2012:chap. 55. Available at: <https://accessmedicine-mhmedical-com.ezproxy.cihe.edu.hk/content.aspx?bookid=392§ionid=41138754>. Accessed January 10, 2019.)



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Clinical Presentation

Pemphigus vulgaris, the most common type, involves the mucosa and skin, especially of the scalp, face, axilla, groins, trunk, and points of pressure. Patients usually present with painful oral mucosal erosions and flaccid blisters, erosions, crusts, and macular erythema in areas of skin involvement.^{19,30} The primary cell adhesion loss is at the deeper suprabasal layer. (Refer to [Chapter 1](#), Anatomy and Physiology of the Integumentary System, for a review of the skin anatomy.) Pemphigus foliaceus is a milder form of the disease, with the acantholysis occurring more superficially in the epidermis, usually on the face and chest. Paraneoplastic pemphigus, in addition to having different autoantibodies, occurs exclusively on patients who have some type of malignancy, usually a lymphoproliferative disorder (**FIGURE 8-10**). Because of the malignancy, mortality is high in this type of

pemphigus.³⁵

Differential Diagnosis

Diagnosis is confirmed by using immunofluorescence to demonstrate the IgG autoantibodies against the cell surface of intraepidermal keratinocytes.

Medical Management

Medical treatment of all three types consists of high-dose systemic corticosteroids, immunosuppressive agents, and intravenous immune globulin. For patients who have refractory pemphigus vulgaris, a combination of [rituximab](#) and intravenous immunoglobulin therapy has been recommended.³³

Wound Management

Wound management is conservative with the goal of preventing infection and promoting reepithelialization in areas where denuding occurs with the blistering. Flat antimicrobial dressings (eg, Acticoat Flex, Smith & Nephew, Largo, FL) are useful over open areas, and hydrotherapy is beneficial when the disease is widespread and in the crusty phase. Secondary dressings are required for most areas, and can include surgical or fish-net garments. Silicone-backed foam dressings without adhesive borders are also recommended for easy removal of loose necrotic tissue without causing painful skin tears.

Bullous Pemphigoid

Pathophysiology

Bullous pemphigoid (BP) is subepidermal autoimmune blistering disease associated with tissue-bound and circulating autoantibodies directed against BP antigen 180 (also known as BPAG 2) and BP antigen 230 (also known as BPAG 1), both components of the basement membrane.^{19,36} An immune reaction is initiated by the formation of IgG autoantibodies that target dystonin, a component of the hemidesmosomes, resulting in the infiltration of immune cells to the area. The consequence is separation of the dermal/epidermal junction with fluid collection and blistering or bullae. The severity of the disease is IgE dose dependent and correlates with the degree of eosinophil infiltration in the skin.³⁷

Clinical Presentation

BP occurs most commonly among the elderly, and the most common sites of involvement include inner aspects of thighs, flexor aspects of forearms, axilla, groin, and oral cavity. The extremities can also become involved. Itching is the first dominating symptom of BP, which progresses to urticarial lesions, erythematous edema, papules, eczematous lesions, and typically widespread tense bullae filled with clear fluid ([FIGURE 8-11](#)).³⁶

FIGURE 8-11

Bullous pemphigoid Tense bullae filled with clear fluid (a result of the inflammatory process) are typical of bullous pemphigoid.



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Differential Diagnosis

Histologically, BP is the prototype of a subepidermal bullous disease along with eosinophilic spongiosis. The dermis shows an inflammatory infiltrate composed of neutrophils, lymphocytes, and eosinophils. Diagnosis is confirmed by the presence of linear deposits of IgG and/or C3 along the dermal-epidermal junction on direct immunofluorescence and IgG class circulating autoantibodies that bind to the epidermal (roof) side of the skin basement membrane on indirect immunofluorescence.^{18,19,38}

Medical Management

Anti-inflammatory agents (corticosteroids, tetracyclines, [dapsone](#)) and immunosuppressants ([azathioprine](#), [methotrexate](#), [mycophenolate mofetil](#), [cyclophosphamide](#)) are the most commonly used medications for BP, usually for 6–60 months, after which most patients will have long-term remission. Longer treatment may be required for patients who have chronic BP.³⁹

Wound Management

Wound management recommendations are the same as for pemphigus, with the goal of minimizing pain, preventing infection, and promoting re-epithelialization.

Cryoglobulinemia

Pathophysiology

Cryoglobulins are abnormal proteins (immunoglobulins), and cryoglobulinemia is the presence of these proteins in the blood. They coagulate or become thick and gel-like in temperatures below body temperature (37°C), thereby clogging the small blood vessels and resulting in vasculitic damage that causes hypoxic skin changes, ischemic wounds, and/or other organ damage ([TABLE 8-8](#)). The symptoms may be reversible if the environmental temperature is warmed. The disorder is grouped into three main types, depending on the type of antibody that is produced: Type I (usually with monoclonal IgM) is most often related to cancer of the blood or immune system, for example, multiple myeloma; Types II and III (polyclonal IgG), also referred to as mixed cryoglobulinemia, most often occur in people who have a chronic inflammatory condition, for example, hepatitis C, Sjögren syndrome, or systemic lupus erythematosus.⁴⁰ Type II is the most common type, and most of these patients also have hepatitis C.^{1,18,19}

TABLE 8-8

Symptoms of Cryoglobulinemia

| Local/Integumentary | General/Systemic |
|---|--|
| <p>Type I</p> <ul style="list-style-type: none"> Lesions in head and mucosa Acrocyanosis Severe Raynaud's phenomenon Digital ulceration Skin necrosis Livedo reticularis Purpura <p>Types II and III</p> <ul style="list-style-type: none"> Lesions in lower extremities Erythematous macules Palpable purpura Raynaud phenomenon Cutaneous vasculitis Peripheral neuropathy Nailfold capillary abnormalities | <p>Type I</p> <ul style="list-style-type: none"> Retinal hemorrhage Arterial thrombosis Renal disease <p>Types II and III</p> <ul style="list-style-type: none"> Breathing difficulty Fatigue Arthralgia (PIP, MCP, knees, ankles) Myalgia Immune complex deposition Cough Pleurisy Abdominal pain Fever Hepatomegaly or signs of cirrhosis Hypertension |

Data from Edgerton CC, Diamond HS. Cryoglobulinemia clinical presentation. Available at: <http://emedicine.medscape.com/article/329255>. Accessed July 27, 2018.

Clinical Presentation

Symptoms vary depending on the type of cryoglobulinemia present and the organs that are affected. Systemic signs that occur with Types II and III may include difficulty breathing, fatigue, glomerulonephritis, joint pain, and muscle pain. Integumentary signs may begin with purpura and Raynaud's phenomenon (**FIGURE 8-12**). The Meltzer triad which is associated with Types II and III includes arthralgia, purpura, and weakness.⁴¹ See **TABLE 8-8** for a list of cryoglobulinemia symptoms.

FIGURE 8-12

Cryoglobulinemia Cryoglobulinemia on the foot of a patient with hepatitis C. Classic signs include purpura, loss of dermis due to occlusion of the small vessels to the skin, severe pain, and tendency to develop infections. This patient's wounds healed with the use of antibiotics and standard wound care; however, when he returned to a cold climate his symptoms recurred.



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Differential Diagnosis (partial list)

- Antiphospholipid syndrome
- Chronic lymphocytic leukemia
- Churg–Strauss syndrome
- Cirrhosis
- Giant cell arteritis
- Systemic lupus erythematosus
- Vasculitis

Medical Management

The goal of treating cryoglobulinemia is to treat the underlying cause (which will often treat or prevent cutaneous symptoms) and to limit the precipitant cryoglobulin and subsequent inflammatory effects. Simply avoiding cold temperatures can treat mild cases. Standard hepatitis C treatments usually work for patients who have hepatitis C and mild or moderate cryoglobulinemia. However, the condition can return when treatment stops. NSAIDs may be used to treat mild cases that involve arthralgia and myalgia. Severe cryoglobulinemia (involving vital organs or large areas of skin) is treated with corticosteroids, immunosuppressants, interferon, or cytotoxic medications. Plasmapheresis may be indicated if the complications are life threatening.^{40–42}

Wound Management

Wound care involves treatment of infection and pain management, especially in the early stages. Nonadherent dressings such as X-Cell (Medline, Mundelein, IL), hydrogel, Acticoat (Smith & Nephew, Largo, FL), and petrolatum gauze help minimize pain with dressing changes and promote autolytic debridement. A topical anesthetic is advised 10 to 15 minutes before initiating any sharp debridement; enzymatic debridement may also be beneficial but can cause stinging and burning upon application. Absorbent dressings are advised if there is wound drainage, and modified compression (eg, with short stretch bandages) helps reduce the edema that occurs with chronic inflammation, immobility, and lower extremity dependency. Compression bandages also help keep the extremities warm and facilitate vasodilation. If edema is not severe, warm hydrotherapy can help reduce precipitation of the cryoglobulins and relieve ischemic pain. Patient education regarding avoidance of cold or wearing warm clothing such as thermal socks is a crucial component of long-term management.

Pyoderma Gangrenosum

Pathophysiology

Pyoderma gangrenosum (PG) is an autoimmune disorder of unknown etiology that leads to painful skin necrosis. PG is commonly associated with other inflammatory diseases such as Crohn's disease, inflammatory bowel syndrome, arthritis, and hematologic malignancy.⁴² Pathergy, the development of skin lesions in the area of trauma or the enlargement of initially small lesions, is commonly seen with PG, especially if debridement of necrotic tissue is attempted. Neutrophilic dermatosis occurs with altered neutrophilic chemotaxis and is thought to be part of the pathology.²²

Clinical Presentation

PG ulcers usually begin as small pustules or blisters (termed cat's paw appearance⁴³) and become larger with a violaceous border and surrounding erythema. The first lesion may be at the site of minor trauma, but will progress and enlarge rapidly. Often the wound edge is undermined. They are painful, necrotic, and usually recurring. Sometimes PG will appear in groups of lesions at different stages of formation or healing. They do not respond to standard care if diagnosed as another wound type, and indeed may worsen if the standard TIMEO₂ care, particularly aggressive debridement, is administered (FIGURES 8-13 to 8-15). The following variants of PG have been identified:

- Classic PG—commonly seen on the lower extremities; scars are often cribriform; patient complains of fever, malaise, arthralgia, and myalgia.
- Peristomal PG—occurs close to abdominal stomas, usually in patients with IBD, ileostomies, or colostomies for malignancy; may have bridges of epithelium that traverse the ulcer base.
- Pustular PG—commonly seen on the trunk and extremity extensor surfaces of patients with IBD; stalls at the pustular stage and may persist for months.
- Bullous PG—commonly seen on upper limbs and face; associated with hematologic conditions with poor prognosis; presents as concentric bullous areas that spread rapidly.
- Vegetative PG—less aggressive and more superficial; may respond well to local treatment.^{19,43,44}

FIGURE 8-13

Pyoderma gangrenosum Pyoderma gangrenosum on the abdomen of a female with diabetes. The PG developed after an open hysterectomy. The wounds were treated with nonadherent antimicrobial dressings (X-cell, Medline Industries, Inc., Mundelein, IL) in order to minimize pain, facilitate autolytic debridement and re-epithelialization, and prevent infection. As the necrotic plaques loosened and new skin was visible beneath, they were removed with sterile forceps; however, aggressive debridement was contraindicated.



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FIGURE 8-14

Pyoderma gangrenosum Some of the characteristics of PG are seen on this lower extremity wound, including the violaceous border, purulence, and necrotic tissue. (Used with permission from Usatine RP. Pyoderma Gangrenosum. In: Usatine RP, Smith MA, Chumley H, Mayeaux, Jr. E, Tysinger J, eds. *The Color Atlas of Family Medicine*. 2nd ed. New York, NY: McGraw-Hill; 2013:chap. 174. Available at:

<http://accessmedicine.mhmedical.com.ezproxy.cihe.edu.hk/content.aspx?bookid=685§ionid=45361241>. Accessed January 10, 2019.)



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FIGURE 8-15

Pyoderma gangrenosum The clinical appearance of PG can vary, as in this wound with both eschar and purulent subcutaneous tissue at the edges. (Used with permission from Usatine RP. Pyoderma Gangrenosum. In: Usatine RP, Smith MA, Chumley HS, Mayeaux EJ, Jr, eds. *The Color Atlas of Family Medicine*. 2nd ed. New York, NY: McGraw-Hill; 2013:chap. 174. Available at: <http://accessmedicine.mhmedical.com.ezproxy.cihe.edu.hk/content.aspx?bookid=685§ionid=45361241>. Accessed August 02, 2018.)



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Differential Diagnosis

As there is no diagnostic test to confirm PG and multiple other conditions that resemble PG, a correct diagnosis relies on clinical presentation and exclusion of other causes. **TABLE 8-9** lists the systemic diseases most often associated with PG. Differential diagnosis includes infections, malignancy (squamous cell or cutaneous lymphoma), vascular lesions, and antiphospholipid syndrome.

TABLE 8-9

Systemic Diseases Associated with Pyoderma Gangrenosum

| Inflammatory Bowel Disease | Arthritis | Hematologic Abnormalities | Immunologic Abnormalities |
|---|---|---|--|
| Ulcerative colitis Regional enteritis Crohn's disease | Seronegative arthritis Rheumatoid arthritis Osteoarthritis Psoriatic arthritis | Myeloid leukemia, hairy cell leukemia, myelofibrosis, myeloid metaplasia, immunoglobulin A monoclonal gammopathy, polycythemia vera, paroxysmal nocturnal hemoglobinuria, myeloma, and lymphoma | Systemic lupus erythematosus Complement deficiency Hypogammaglobulinemia Hyperimmunoglobulin E syndrome Acquired immunodeficiency syndrome |

Medical Management⁴⁵

Systemic management includes treatment of any underlying disease and long-term immunosuppression with high doses of corticosteroids or low doses of cyclosporin.^{43,45} Other therapies that have been used in patients with PG include antibiotics (**dapsone** and **minocycline**), **clofazimine**, **azathioprine**, **methotrexate**, **chlorambucil**, **cyclophosphamide**, **thalidomide**, **tacrolimus**, **mycophenolate**, mofetil, IV immunoglobulin, plasmapheresis, and infliximab.^{18,19,46}

Wound Management

Topical steroids, topical [tacrolimus](#), [nicotine](#) patches, and intralesional steroids have been used for mild or moderate disease. *Debridement of adhered tissue is contraindicated and may cause pathergy*; however, as the necrotic tissue loosens with re-epithelialization, it may be gently removed with sterile forceps. Keeping the lesions covered with a nonadherent mesh or silicone-backed wicking foam that will allow drainage to escape to a secondary dressing can help alleviate the pain associated with PD wound care. Maggot therapy has been successfully used in some cases. Split-thickness skin grafts, along with concurrent immunosuppressive therapy to reduce the risk of pathergy, have been reported. Alternative therapies include application of bioengineered skin and hyperbaric [oxygen](#) therapy.⁴⁷

Necrobiosis Lipoidica

Pathophysiology

Necrobiosis lipoidica (previously referred to as *necrobiosis lipoidica diabetorum*) is a [collagen](#) disorder of unknown etiology that is usually seen in morbidly obese patients with a strong family history of diabetes; however, not all patients have diabetes, therefore the change in nomenclature.⁴⁸ Different pathological mechanisms have been proposed and include (1) diabetic microangiopathy as a result of glycoprotein deposition in the blood vessels, (2) abnormal [collagen](#) degeneration, (3) deposition of immunoglobulins in the blood vessel walls with enhanced platelet aggregation and coagulation, and (4) impaired neutrophil migration leading to an increased number of macrophages and subsequent granuloma formation.⁴⁹ Necrobiosis lipoidica also results in thickening of the blood vessel walls and fat deposition, making the integumentary symptoms similar to vasculitis. The disease tends to be chronic with recurrent lesions and scarring,⁴⁶ and carries an associated risk of the development of squamous cell carcinoma.⁵⁰

Clinical Presentation

Lesions usually are bilateral but asymmetric on the tibial surface of the lower leg, and begin as a rash or 1–3 mm slightly raised spots. They progress to irregular ovoid reddish-brown plaques with shiny yellow centers and violaceous indurated borders. The edges may be raised and purple, and the wound bed may have good granulation tissue but no epithelial migration. Pain and edema are also usually present. Remodeling is characterized by round patches of hyperpigmentation (**FIGURE 8-16**).^{18,19,51} Direct immunofluorescence microscopy of necrobiosis lipoidica reveals IgM, IgA, C₃, and fibrinogen in the blood vessels which will cause vascular thickening.⁴⁹

FIGURE 8-16

Necrobiosis lipoidica diabetorum NLD lesions are characterized by symmetrical tan-pink or yellow plaques with well-demarcated, raised borders and depressed, atrophied centers. Telangiectasia is also visible throughout the wound. (Used with permission from Jameson J. Atlas of clinical manifestations of metabolic diseases. In: Jameson J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York, NY: McGraw-Hill. Available at: <http://accessmedicine.mhmedical.com.ezproxy.cihe.edu.hk/content.aspx?bookid=2129§ionid=192509587>. Accessed July 28, 2018.)



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Differential Diagnosis

- Pyoderma gangrenosum
- Calciphylaxis
- Vasculitis
- Diabetic wound with peripheral vascular disease
- Granuloma annulare (Binkley's spots)
- Sarcoidosis
- Necrobiotic xanthogranuloma

Medical Management

Systemic steroids or other immunotherapy can be given to patients with severe disease. Cutaneous blood enhancers such as [pentoxifylline](#) and [aspirin](#) may be helpful in facilitating cell migration to the damaged tissue and inhibiting platelet aggregation.⁴⁹ Cyclosporin,⁵² mycophenolate,⁵³ and infliximab⁵⁴ have also been reported to successfully treat necrobiosis lipoidica.

Wound Management

Topical and intralesional steroids can be beneficial in treating mild to moderate cases. Other reported treatments include 0.1% topical **tacrolimus** ointment,^{48,51} **collagen** matrix dressings,⁵⁵ and phototherapy.⁵⁶ A combination of low-frequency noncontact ultrasound, topical steroid ointment, saline-impregnated **cellulose** dressings, and multilayer compression wraps, in conjunction with **pentoxifylline**, was a successful combination used by the author for a patient with chronic lesions of more than 1 year duration.

HERPES VIRUS

Varicella is a virus that presents in three different ways: herpes simplex Type 1 (oral or cold sores), herpes simplex Type 2 (genital herpes), and herpes zoster (chicken pox and shingles).

Pathophysiology

The *herpes simplex virus* (HSV) persists in an individual for a lifetime due to the presence of a latent pool of the virus in terminally differentiated neurons, usually the peripheral ganglion.⁵⁷ HSV is a DNA virus that invades the cell nucleus and replicates, thereby producing partial thickness wounds. Herpes simplex Type 1 activation is commonly referred to as “cold sores” that occur on the mouth and lips. (**FIGURE 8-17**). Herpes simplex Type 2 is recognized as a sexually transmitted disease that results in lesions on the genital skin. Both can be reactivated, and in immune-compromised individuals can lead to local infection, chronic herpetic ulcers, and mucous membrane damage, as well as systemic infections in the central and peripheral nervous systems, the gastrointestinal tract, and the ocular system.⁵⁸

FIGURE 8-17

Herpes simplex virus Type 1 Herpes simplex is commonly known as a cold sore.



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Chicken pox is a childhood disorder caused by the *varicella-zoster virus* (VZV). The virus enters through the respiratory system and infects the tonsillar T cells. The infected T cells carry the virus to the reticuloendothelial system where the major replication occurs and to the skin where the rash appears (**FIGURE 8-18**).⁵⁹

FIGURE 8-18

Herpes zoster, chicken pox The dermal lesions associated with chicken pox begin as a rash and rapidly progress through the stages of papules, vesicles, pustules, and crusts. (Used with permission from Schmader KE, Oxman MN. Varicella and herpes zoster. In: Goldsmith LA, Katz SI, Gilchrist BA,

Paller AS, Leffell DJ, Wolff K. eds. *Fitzpatrick's Dermatology in General Medicine*. 8th ed. New York, NY: McGraw-Hill; 2012:chap. 194. Available at: <https://accessmedicine-mhmedical-com.ezproxy.cihe.edu.hk/content.aspx?bookid=392§ionid=41138923>. Accessed January 10, 2019.)



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The VZV can remain latent in the nerve ganglion and reactivate in later years, usually during a period of stress or immunosuppression, as herpes varicella-zoster or “shingles” (FIGURE 8-19A, B). Vesicles can involve the corium and dermis, with degenerative changes characterized by ballooning, multinucleated giant cells, and eosinophilic intranuclear inclusions. Infection may involve localized dermal blood vessels, resulting in necrosis and epidermal hemorrhage.¹⁸ Individuals who are immunosuppressed (eg, patients with HIV or transplants) can have more severe cases of herpes, with the incidence of herpes zoster more than 14 times higher in adults with HIV.

FIGURE 8-19

Herpes zoster, shingles Herpes zoster, commonly known as shingles, begins as a rash or small vesicles and progresses to dry eruptions. (A) The pattern follows a specific dermatome, becoming hard dry crusts (B), and usually resolves in 10–15 days although the post-herpetic pain may linger for months to years.



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Clinical Presentation

Herpes simplex usually occurs initially in childhood and progresses through the stages of prodrome, erythema, papule, vesicle, ulcer, hard crust, and residual dry flaking and swelling. Lesions can become secondarily infected by *Staphylococcus* or *Streptococcus*. Individuals tend to have recurrent eruptions. Nonulcerative lesions tend to last 3 days; full-blown ulcerative lesions may last 7–10 days.

Chicken pox usually presents with prominent fever, malaise, and a pruritic rash that starts on the face, scalp, and trunk and spreads to the extremities. The rash is initially maculopapular and rapidly progresses to vesicles, then pustules that rupture, and then to crusts.

Herpes varicella-zoster (HZV) presents as an eruption of grouped vesicles on an erythematous base limited to a single dermatome. Initial symptoms include dermatologic tingling or pain in the affected dermatome 48–72 hours before the onset of lesions, which can appear 3–5 days later. Lesions develop quickly into vesicles, then rupture, ulcerate, and dry out. They usually resolve in 10–15 days, although the pain may remain as post-herpetic neuralgia. In patients with advanced HIV, the herpetic infection may develop into chronic ulcers and fissures with a substantial degree of edema.

Differential Diagnosis

History and clinical presentation are often all that is necessary to establish the diagnosis of herpes; therefore, confirmatory tests such as the Tzanck smear preparation, biopsy, or viral culture are rarely necessary. Other differential diagnoses include:

- Small pox—lesions are deeper and painful; all lesions occur at the same stage

- Disseminated HSV—usually occurs in the setting of a skin disorder
- Meningococemia—presents with petechiae, purpura, and sepsis
- Atopic dermatitis
- Atypical measles
- Poison ivy
- Spinal nerve compression (pain)

Medical Management

Chicken pox will usually heal in less than 2 weeks without medical intervention.

Uncomplicated HZV is treated for 7–10 days with [acyclovir](#) (Zovirax), [famciclovir](#) (Famvir), or [valacyclovir](#) (Valtrex).⁶⁰ These oral antiviral medications reduce the duration and severity of adult symptoms. Oral [prednisone](#) may decrease the risk of post-herpetic neuralgia. VariZIG injections may prevent complications in immune-compromised and pregnant patients, as well as decrease the severity of HZV symptoms.⁶¹ As of October 2017, a new vaccine (Shingrix) is recommended to be administered twice, 2–6 months apart, and is considered 90% effective in preventing shingles and post-herpetic pain.⁶² Antihistamines may help reduce the itching, and Zostrix may help reduce severe neuralgia. If the lesions have not healed in 3–4 weeks, the patient may have a drug-resistant virus that requires treatment with IV [foscarnet](#).

HSV infections are treated with antiviral medications ([Acyclovir](#)); however, long-term use of this medication in immunosuppressed patients can lead to drug resistance, requiring research for a next generation antiviral medication.⁶³

Wound Management

Herpes simplex can be treated with topical [acyclovir](#) and mild corticosteroid ointment⁶⁴ or with a thin hydrocolloid dressing.⁵⁹ Moisture retentive dressings such as hydrogels, hydrocolloids, transparent films, or alginates may be helpful to facilitate autolytic debridement of necrotic tissue and healing of herpes-varicella wounds.

INFECTED WOUNDS (BACTERIAL)

Necrotizing Fasciitis

Pathophysiology

Necrotizing fasciitis (NF) is a deep-seated infection of the subcutaneous tissue that progresses rapidly along fascial planes with severe systemic toxicity and 40% mortality. NF leads to progressive destruction of fascia, subcutaneous fat, and muscles, usually with resulting necrosis of the overlying skin.⁶⁵ Bacteria enter the skin through a cut or scratch; the most common offenders are Group A streptococcus (*Streptococcus pyogenes*), *Staphylococcus aureus*, *Clostridium perfringens*, *Bacteroides fragilis*, *Aeromonas hydrophila*, and *Klebsiella*. NF has been classified into two major categories: Type 1 is polymicrobial involving at least one anaerobe with or without a facultative anaerobe (a microorganism that can live and grow with or without molecular [oxygen](#)) and is localized on the trunk, abdomen, or perineum; Type 2 is monomicrobial, usually caused by group A beta hemolytic streptococci and/or other streptococci or staphylococci and occurs on the extremities.⁶⁵ The bacteria release toxins that produce an exotoxin that in turn activates T cells. This process produces increased cytokines that lead to severe systemic symptoms known as toxic shock syndrome, which can be fatal if the initial necrosis and infection are not immediately controlled.^{1,18}

Risk factors for NF include IV drug use, diabetes, renal failure, pulmonary diseases, liver cirrhosis, peripheral vascular disease, obesity, malnutrition, and drug abuse.⁶⁶ A 50% mortality rate is associated with any combination of three or more risk factors.

Clinical Presentation

NF is frequently preceded by a minor skin trauma that serves as a portal for the causative bacteria (**FIGURE 8-20**). This is followed by a sequence of the following clinical manifestations:

- Low-grade fever
- Pain, usually out of proportion to the initial clinical findings
- Swelling with massive, “sausage-like” edema
- Erythema with bullous skin changes
- Lack of adenopathy, misses immune recognition
- Skin necrosis with hypoesthesia or anesthesia
- Striking indifference to one's clinical state
- Toxic-shock appearance with rapid demise

FIGURE 8-20

Necrotizing fasciitis Necrotizing fasciitis begins with edema and erythema with bullae as a result of the underlying, fast-spreading infection. Any patient suspected of having necrotizing fasciitis requires emergent surgical debridement in order to prevent systemic complications. (Used with permission of Dr. Jayesh Shah.)



Source: Rose L. Hamm: *Text and Atlas of Wound Diagnosis and Treatment*, 2e
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Basic antigen testing may identify *Streptococcus*, but does not establish a diagnosis. A basic rapid strep test is helpful, and polymerase chain reaction testing can help identify streptococcal pyrogenic exotoxin genes (SPE=B).

Differential Diagnosis

- Cellulitis—all of the signs of NF may not be present initially, leading to an early misdiagnosis of cellulitis.
- Gas gangrene—See detailed description on page 251.

Medical Management

Medical management includes appropriate antibiotics, aggressive surgical debridement of all infected subcutaneous and dermal tissue (the saying is that the patient goes straight from the ER to the OR), medical stabilization as needed, and adjunctive hyperbaric oxygen therapy⁶⁷ (discussed in more detail in [Chapter 18](#), Hyperbaric Oxygen Therapy).

Wound Management

Wound management depends on the amount of debridement done surgically, as well as the amount and quality of the residual soft tissue. If there is concern about continued infection, antimicrobial dressings are used, for example, Nanocrystalline [silver](#), half or quarter strength Dakin solution (unless there is granulation tissue), or acetic acid washes for *pseudomonas*. Once the wounds are more than 70% clean, negative pressure wound therapy is useful to facilitate wound contraction and angiogenesis in preparation for skin grafts or flaps.⁶⁸ Pain management during wound care is essential, and if the wounds are extensive, rehabilitation services and/or psychological care may be needed.⁶⁹

Fournier Gangrene

Fournier gangrene is an aggressive form of necrotizing infection of the perineum that may extend to the anterior abdominal wall, gluteal muscles, and in males, to the penis and scrotum. The causative organisms are a mixed collection of aerobic gram-negative bacteria, enterococci, and anaerobes, including bacteroides and peptostreptococci.⁷⁰ Medical and wound management include the strategies for any necrotizing fasciitis.

Myonecrosis (Gas Gangrene)

Pathophysiology

Myonecrosis, also known as gas gangrene, occurs after a deep penetrating injury compromises the blood supply, thus creating the anaerobic conditions ideal for infection.^{18,19} The majority of the infections in this situation are caused by *Clostridium perfringens*, although other species of *Clostridium* have been implicated. *C. perfringens* produce multiple toxins (including bacterial proteases, phospholipases, and cytotoxins) that cause aggressive necrosis of the skin and muscles.⁷¹ The same bacteria can cause clostridial cellulitis, which also occurs after trauma or surgery. Known risk factors for developing myonecrosis are essentially the same as for any necrotizing soft-tissue infection, especially immunosuppression, diabetes, cancer, and vascular disease.⁷²

Clinical Presentation

The patient presents with severe pain, and the skin changes color from pale to bronze to purplish-red with bullae formation. Gas in the tissue is evident from physical examination as crepitus upon palpation or by radiography. **TABLE 8-10** presents a detailed list of integumentary signs and symptoms associated with gas gangrene (**FIGURE 8-21**). In addition, renal failure may occur as a result of hemoglobinuria and myoglobinuria, as well as bacteremia and hemolysis. The patient may rapidly progress to shock and multiorgan failure with toxic psychosis.

FIGURE 8-21

Myonecrosis (gas gangrene) Myonecrosis of the foot after trauma with subsequent clostridial infection. The collection of gas causes the bullous on the dorsum of the foot. Pockets of myonecrosis that form in deep tissue will expel an odor of gas when opened during debridement. (Used with permission from Tubbs RJ, Savitt DL, Suner S. Extremity conditions. In: Knoop KJ, Stack LB, Storrow AB, Thurman RJ, eds. *The Atlas of Emergency Medicine*. 3rd ed. New York, NY: McGraw-Hill; 2010:chap. 12. Available at <https://accessmedicine-mhmedical-com.ezproxy.cihe.edu.hk/content.aspx?bookid=351§ionid=39619711>. Accessed January 10, 2019.)



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TABLE 8-10

Integumentary Signs and Symptoms of Gas Gangrene

| Early Signs and Symptoms | Skin Changes | Late Signs and Symptoms | Other Findings |
|--|---|--|---|
| Incubation period of about 48 hours Fever Pain out of proportion to injury Tachycardia Diaphoresis Gray Pallor Anoxemia Apprehension Disorientation Obtundation | Shiny and tense skin Tense, bronzed, and tender skin Blue-black bullae Gas and crepitation Odor | Myonecrosis Hemolytic anemia Hematuria Myoglobinuria Acute renal failure Metabolic acidosis Consumptive coagulopathy Seizures and death | Ischemia and inoculation Bacterial proliferation Exotoxin production Tissue destruction Edema and necrosis Decreased redox potential Gangrene Hemorrhagic bullae Gas in muscles |

Medical Management

Medical management of gas gangrene is predicated on debridement of all devitalized and infected tissue and appropriate IV antibiotics. Adjunctive hyperbaric [oxygen](#) therapy is recommended to control infection and decrease further extension of necrosis.⁷³

Wound Management

Initial local wound care is packing or covering with antiseptic or antimicrobial dressings using aseptic precautions. When healthy tissue is visible, the principles of moist wound healing are followed and may include the use of negative pressure wound therapy to help decrease the size of tissue defect caused by surgical debridement.

Actinomycosis

Pathophysiology

Actinomycosis is caused by a gram-positive, nonspore forming anaerobic bacilli, the most common being *Actinomycosis israelii* which is normally found in the nose, throat, and genital tract.⁷⁴ The most common locations for infections are cervicofacial, abdominal, or thoracic; however, actinomycosis on the foot has also been reported.^{75,76} Cervicofacial actinomycosis can also be associated with local tissue damage caused by neoplastic conditions and irradiation. The infection is usually accompanied by the presence of some other bacteria that facilitates its invasion of tissue.⁷⁷

Clinical Presentation

The clinical presentation of actinomycosis, which is usually chronic and difficult to eliminate, varies with the location. Cervicofacial actinomycosis develops slowly; the area becomes markedly indurated and the overlying skin becomes reddish or cyanotic. In addition, the wound may produce particles (similar to, and frequently called, sulfur particles because of their yellow color)⁷⁴ that carry the bacteria, frequently into adjacent soft tissue and bone (FIGURE 8-22). Pulmonary actinomycosis occurs in individuals with poor oral hygiene, preexisting dental disease, alcoholism, and chronic lung disease; it begins with fever, cough, and sputum production.⁷⁴ Other signs include night sweats, weight loss, and pleuritic pain. Abdominal actinomycosis usually causes pain in the ileocecal region, spiking fever and chills, vomiting, and weight loss.⁷⁸ This type may be confused with Crohn's disease.

FIGURE 8-22

Actinomycosis Clinical signs of actinomycosis include the white particles that accumulate on the wound surface and induration and edema of the periwound tissue, resulting in deformity of the structure. This patient had a history of two surgeries to remove a tumor from the suborbital area, and ultimately had surgical removal of the infected tissue with plastic reconstruction.



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Differential Diagnosis

- Nocardiosis
- Madura Foot
- Cellulitis

Medical Management

Surgical excision is usually required for actinomycosis, and IV or oral antibiotics (beta-lactams such as [ampicillin](#), penicillin, or [amoxicillin](#)) are recommended for 6 months. [Doxycycline](#) and sulfonamides may also be used; however, medical treatment is slow.⁷⁸

Wound Management

Actinomycosis is treated locally with antibiotic solutions or with local antibiotic cream or anti-infective agents.

Mycobacteria

Pathophysiology

Mycobacteria can be typical or atypical, and the bacteria are neither gram positive nor gram negative. Atypical strains were not reported as human pathogens until the 1950s. Mycobacterial cutaneous infections usually result from exogenous inoculations, and predisposing factors include a history of preceding trauma, immunosuppression, or chronic disease, especially diabetes. [TABLE 8-11](#) presents a list of mycobacteria, as well as their clinical presentations and treatments.^{79,80}

TABLE 8-11

Mycobacterium Species That Cause Integumentary Disorders

| Species | Clinical Presentation | Treatment |
|---|--|---|
| <i>Mycobacterium tuberculosis</i> species Scrofuloderma Lupus vulgaris Military lesions | Abscess Lymphadenopathy Fistulae Ulcerations | Surgery Antituberculous drugs |
| Nontuberculous mycobacteria <i>M. marinum</i> <i>M. ulcerans</i> (Buruli ulcer) | Swimming pool and fish tank granuloma Subcutaneous nodule | Antituberculous drugs Surgical excision |
| <i>M. avium intracellulare</i> <i>M. kansasii</i> <i>M. chelonae</i> <i>M. fortuitum</i> | Small ulcers with erythematous borders Crusted ulcerations Painful nodules, abscesses, surgical wound infection Painful nodules, abscesses, surgical wound infections | Surgical excision and chemotherapy Antituberculous drugs, minocycline Erythromycin , tobramycin , amikacin , doxycycline Amikacin , doxycycline , ciprofloxacin , sulfamethoxazole |

Clinical Presentation

The cutaneous lesions vary depending on the causative agent and may present as granulomas, small superficial ulcers, sinus tracts, abscesses, or large ulcerated lesions localized in exposed areas. The appearance is very similar to lesions seen in leprosy and may be difficult to differentiate. Tissue cultures are required to make an accurate diagnosis of any mycobacterial infection.

Medical Management

The primary medical treatment of mycobacterial infections is specific chemotherapy, the major ones being [Isoniazid](#) (INH) and Rifampicin (RMP). Other first-line medications are [pyrazinamide](#), [ethambutol](#), and streptomycin.^{81,82} Drug resistance is a global problem and numerous second-line defense

medications have been presented in the literature.

Wound Management

Wound management is based on use of antimicrobial dressings, management of exudate, and use of aseptic technique to prevent further infection. Use of airborne precautions by all care-givers is required if the strain is tuberculin.

Osteomyelitis

Pathophysiology

Osteomyelitis, or infection of the bone, derives its name from *osteo* (meaning bone) and *myelo* (relating to myeloid tissue in the bone marrow). Osteomyelitis can be acute (diagnosed within 2 weeks of onset of signs and symptoms) or chronic (reoccurs in a patient with a history of osteomyelitis).⁸³ It can be further classified as hematogenous (caused by pathogens carried in the blood stream from sites of infection in other parts of the body) or exogenous (caused by pathogens that enter from outside the body, eg, from open fractures, surgical sites, and penetrating wounds).⁸⁴ Acute hematogenous osteomyelitis occurs most frequently in children, especially those with sickle cell disease, and affects the long bones (femur, tibia, humerus, pelvis). Chronic osteomyelitis occurs most frequently in adults, especially those with diabetes, open fractures, implanted hardware, and vascular insufficiency. In the diabetic population with vascular insufficiency, the bones most affected are the small bones in the foot.⁸³

The sequence of osteomyelitis involves the following stages: Stage 1—the pathogen, usually *Staphylococcus aureus*, invades the medullary canal of the bone and becomes a nidus of infection; Stage 2, the acute phase—the infection results in pus from the inflammatory process and spreads to the vascular channels in the bone; and Stage 3, the chronic phase—the inflammatory process obliterates the vascular channels with subsequent ischemia and bone necrosis.⁸³ The pieces of necrotic bone may separate from the healthy bone (termed sequestrum), and can occur on any infected bone (FIGURE 8-23).

FIGURE 8-23

Osteomyelitis of the sacrum The exposed bone in this sacral pressure ulcer has chronic osteomyelitis with necrosis and sequestrum of the cortical layer of the bone.



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Clinical Presentation

Acute hematogenous osteomyelitis usually presents with focal tenderness, swelling, or difficulty with weight-bearing activities, especially in the lower extremities. The clinical diagnosis is supported by acute inflammatory serum studies (including white blood cell count, ESR, C-reactive protein) along with radiologic studies.⁸³ MRI studies and technetium 99 m bone scans are very sensitive, and a definitive diagnosis is made with biopsies. Although X-rays may not be definitive until 10–14 days after onset of symptoms, they will show edema in the adjacent soft tissue and areas of sclerosis.

Osteomyelitis in adult patients usually occurs with surgical reduction and internal fixation of fractures, prosthetic devices, open fractures, and soft tissue infections. The symptoms will usually occur about 1 month after introduction of the pathogen, and include low-grade fever, drainage, pain, and loss of bone stability. The overlying soft tissue may be edematous, erythematous, or necrotic. Exposed bone in the wound bed, a positive “probe-to-bone” test, or a wound more than 2 cm² on the foot of a patient with diabetes is very suspicious of underlying osteomyelitis (FIGURE 8-24).⁸⁵ Bone biopsy confirms osteomyelitis and identifies the specific pathogen; however, increased leukocyte count, ESR greater than 70 mm/h, and plain films provide 89% sensitivity and 88% specificity.⁸⁶

FIGURE 8-24

Chronic osteomyelitis in a diabetic foot Signs of osteomyelitis in the foot of a patient with diabetes include open tunneling wounds, positive probe-to-bone test, edema, erythema, “sausage” appearance of the 5th toe, and patient complaints of pain with weight-bearing. Note the discoloration of the skin which is an indication of the extent of subcutaneous soft tissue damage.



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Medical Management

The mainstay of treatment for all cases of osteomyelitis is identification of the pathogen, through biopsy or surgical debridement, and specific antibiotics for at least 6 weeks. For patients with diabetes, antibiotics for up to 12 weeks have been recommended.⁸³ Surgical debridement is advised for a wound that includes tissue invasion, abscess, open purulence, fistulae, or acute osteomyelitis, all of which could lead to sepsis. Amputation, foot reconstruction, osteotomies, or musculocutaneous flaps may be required in severe cases of chronic osteomyelitis. A thorough vascular assessment is vital for any patient with a history of peripheral vascular disease. (See [Chapter 4](#), Vascular Wounds.)

Wound Management

Wounds are treated with standard moist wound care both before and after surgical debridement, which may include topical antimicrobial dressings, absorbent dressings until drainage abates, and off-loading strategies for any plantar foot wound. Negative pressure wound therapy may be used for post-surgical open wounds with adequate vascular supply, and hyperbaric [oxygen](#) therapy may be helpful for patients with diabetes and marginal blood supply. (See [Chapter 18](#).)

INFECTED WOUNDS (FUNGAL)

Sporotrichosis

Pathophysiology

Sporotrichosis is a subacute or chronic fungal infection caused by the fungus *Sporothrix schenckii*, which occurs as a consequence of traumatic implantation of the fungus into the skin. It is usually seen in nursery workers, florists, and gardeners who have exposure to soil, sphagnum moss, or decaying wood.⁸⁷

Clinical Presentation

The patient usually presents with nontender, red maculopapular granulomas, usually 2–4 mm in diameter, which may ulcerate ([FIGURE 8-25](#)). The primary lesion is typically painless and may be surrounded by raised erythema.⁸⁸ It is often associated with lymphangitis; less often inhalation of the

fungus can lead to pulmonary infection and subsequently spread to the bones, eyes, central nervous system, and viscera.

FIGURE 8-25

Sporotrichosis Cutaneous lesions of sporotrichosis are characterized by erythema around the primary wound. The sloughing of the epidermis is a result of the inflammatory response in the periwound skin. (Used with permission from Zafren K, Thurman RJ, Jones ID. Environmental Conditions. In: Knoop KJ, Stack LB, Storrow AB, Thurman RJ, eds. *The Atlas of Emergency Medicine*. 3rd ed. New York, NY: McGraw-Hill; 2010:chap. 16. Available at: <https://accessmedicine-mhmedical-com.ezproxy.cihe.edu.hk/content.aspx?bookid=351§ionid=39619716>. Accessed January 10, 2019.)



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Differential Diagnosis

- Other fungal infections
- Brown recluse spider bite

Medical Management

Sporotrichosis is usually treated with systemic medications, including saturated solution of potassium iodide, [itraconazole](#), [fluconazole](#), [terbinafine](#), and amphotericin B.

Wound Management

Local wound management includes topical antifungal agents, topical application of saturated solution of potassium iodide, and topical application of heat (the sporotrichosis organism grows at low temperatures).

Tinea infections

Pathophysiology

Tinea infections are specific fungal infections caused by dermatophytes that obtain their nutrition exclusively from keratin (eg, stratum corneum, hair, and nails).⁸⁹ The most common tinea infections are caused by epidermophyton, trichophyton, or microsporum.⁹⁰

Clinical Presentation

Clinical signs of fungal infections are scaly skin, erythematous plaques, and annular plaques. A definitive fungal odor may sometimes be present. Rarely are the lesions vesicular or pustular. The specific disorder is named according to the body part infected as follows: tinea capitis (scalp, eyelashes, eyebrows), tinea barbae (beard), tinea corporis (skin not covered by other nomenclature, commonly known as *ringworm*), tinea cruris (genital area), tinea manus (hand), tinea pedis (feet), and tinea unguium or onychomycosis (nails). Onychomycosis is characterized by thick yellow nails due to hyperkeratosis of the undersurface of the nail, yellow or chalky-white discoloration, longitudinal folds in the nail bed, accumulation of debris under the nail causing the nail to separate from the nail bed, crumbly distortion of the nail, and possible loss of the nail. Onychomycosis is frequently observed on the diabetic foot (FIGURES 8-26 to 8-28). Tinea corporis may occur under compression bandages if the skin tends to be moist, and candidiasis (a yeast-like fungus caused by *Candida albicans*) can affect the mucous membranes, the gastrointestinal tract, and vagina (frequently seen on the skin of patients with urinary infections).⁹¹

FIGURE 8-26

Tinea capitis Symptoms of tinea capitis include patches of hair loss, “black dot” pattern within the patches, broken-off hairs, scaling, and itching.



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FIGURE 8-27

Tinea pedis Fungal infection of both the nails and the skin is visible on this foot. It is frequently accompanied by a distinctive odor and usually has to be treated with oral medications.



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FIGURE 8-28

Onychomycosis Debris from the fungi on the toe nails, termed onychomycosis, causes the nail to become thick and yellow. The debris under the nail causes it to lift off the nail bed and frequently the nail will detach itself.



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Differential Diagnosis

Histological features of tinea infections include neutrophils in the stratum corneum, often with parakeratosis and a variable inflammatory response in the dermis. The organisms are best visualized by histological biopsy with periodic acid-Schiff (PAS) staining and potassium hydroxide (KOH) prep may show branching septate hyphae.¹⁹

Medical Management

Systemic treatment with antifungal agents such as [fluconazole](#) is used for severe cases only. Oral [itraconazole](#) and [terbinafine](#) are recommended for onychomycosis and tinea capitis.⁹²

Wound Management

The mainstay of treatment for fungal infections is topical antifungal creams, for example, imidazoles, triazoles, and allylamines. They are applied twice daily and application needs to continue for a week after symptoms have resolved. Topical treatment of onychomycosis may take several months before visible changes in the nail can be observed.

MALIGNANT WOUNDS

Basal Cell Carcinoma

Pathophysiology

Basal cell carcinoma is the most common type of skin cancer affecting one in every six Americans. The neoplasm arises from damaged undifferentiated basal cells as a result of prolonged exposure to ultraviolet (sun) light. The UV exposure leads to the formation of thymine dimers, a form of DNA damage. BCC occurs when the DNA damage is greater than what the cells can naturally repair.⁹³

Clinical Presentation

BCC presents as a small pearly-white, scaly wound that outgrows its blood supply, eventually erodes, and subsequently ulcerates. Other characteristics include prominent telangiectatic surface vessels, rolled edges, or a slightly raised or dome-shape, as well as being painless and slow growing.⁹⁴ BCC usually occurs on the head, neck, back, or chest where there has been sun exposure. Multiple variants include superficial, infiltrative, and nodular basal cell carcinoma (with papules present) ([FIGURE 8-29](#)).

FIGURE 8-29

Basal cell carcinoma Basal cell carcinoma is the least dangerous of the skin cancers but can become large ulcerated lesions if not removed early.



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Differential Diagnosis

- Squamous cell cancer

- Vasculitis

Medical Management

Treatment consists of biopsy to confirm the diagnosis and excision of the lesion with curettage, electrodesiccation, or Mohs micrographic surgery.⁹⁵ Close follow-up with full-body skin inspection by a dermatologist or other medical specialist is advised for early detection of additional lesions that may occur. Superficial, primary BCC can be treated non-invasively with 5% [imiquimod](#) cream.⁹⁶

Wound Management

Wound management is not usually indicated unless an excision becomes infected or for some other reason fails to heal. In such a case, moist wound healing is recommended. Cleansing with hydrogen peroxide is contraindicated as it is cytotoxic, has no antibacterial properties, and can instead prevent wound closure.

Patient education regarding avoidance of sun exposure is necessary for prevention of further lesions.

Squamous Cell Carcinoma

Pathophysiology

Squamous cell carcinoma (SCC), the second most common form of skin cancer, is a malignant neoplasm of the keratinizing epidermal cells with histological evidence of dermal invasion. The development of SCC has been reported in chronic wounds secondary to burns, trauma, hidradenitis suppurativa, radiotherapy, diabetes, and draining sinus tracts of chronic osteomyelitis. Risk factors for SCC include the following: exposure to ultraviolet A and B light, fair skin and blue eyes, radiation therapy, and antirejection medications after organ transplant.⁹⁷ A recent study by Lipper confirmed that the antihypertensive drug [hydrochlorothiazide](#) (HCTZ) is a potent photosensitizer and increases the risk of SCC, especially on the lip, and recommends that patients with other risk factors for SCC be placed on alternative antihypertensive agents.⁹⁸

If the SCC occurs in the area of a previous wound, for example, a burn, venous ulcer, or traumatic wound, years after the initial wounding, it is termed a Marjolin ulcer. This type of SCC is usually very aggressive and requires excision beyond its margins plus radiation therapy.^{99,100}

Clinical Presentation

SCC usually presents as a firm smooth red papule, nodule, or plaque. The edges are poorly defined and the surrounding skin is scaly. It is commonly hyperkeratotic or ulcerated and may metastasize and grow rapidly ([FIGURES 8-30](#) and [8-31](#)).⁹⁴

FIGURE 8-30

Squamous cell carcinoma, early stage Squamous cell carcinoma begins as a hyperkeratotic patch that can ulcerate and metastasize rapidly.



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FIGURE 8-31

Squamous cell carcinoma, late stage Recurrent squamous cell carcinoma can occur at any place on the body; primary lesions can also occur on inner tissue such as the vocal cords, larynx, or esophagus.



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Differential Diagnosis

- Basal cell cancer
- Vasculitis

Medical Management

Smaller, low-risk SCCs are treated with surgical excision, electrodesiccation and curettage, or cryotherapy; larger, high-risk lesions are best treated with Mohs micrographic surgery.⁹⁴ If the SCC metastasizes, chemotherapy and radiation therapy are indicated, as well as excision of nodules and any

regional lymph nodes that are involved.

Wound Management

Because of the chemotherapy and radiation of affected tissue, wounds are not uncommon after excision of SCC. Supportive wound care is required, including infection control, pain management, lymphedema management, and frequent inspection for new lesions. Absorbent antimicrobial dressings are useful in preventing secondary infections, in managing drainage, and in preventing further skin maceration at the wound site.

Melanoma

Pathophysiology

Melanoma, the most lethal form of skin cancer, is a tumor of the melanocytes of the epidermis. **TABLE 8-12** lists the different types of melanoma and **TABLE 8-13** presents the Breslow depth scale, which is used as a prognostic indicator. The scale indicates how deeply the tumor cells have invaded the epidermis/dermis in micrometers.¹⁰¹ The cause of melanoma is exposure to ultraviolet light in the sun and from tanning beds.

TABLE 8-12

Types of Melanoma

Superficial spreading malignant melanoma
Nodular melanoma
Acral lentiginous melanoma
Amelanotic melanoma
Minimal deviation melanoma
Desmoplastic melanoma

TABLE 8-13

Breslow Depth Scale for Melanoma

| Stage | Depth | Depth of Tissue Involvement |
|-----------|----------------------|--|
| Stage I | ≤0.75 mm | Confined to epidermis (<i>in situ</i>) |
| Stage II | 0.75 mm–1.5 mm | Invasion into papillary dermis |
| Stage III | 1.51 mm–2.25 mm | Fills papillary dermis and compresses the reticular dermis |
| Stage IV | 2.25 mm–3.0 mm | Invasion of reticular dermis (localized) |
| Stage V | >3.0 mm ¹ | Invasion of subcutaneous tissue (regionalized by direct extension) |

The Breslow depth scale is a prognostic indicator for melanoma based on the depth of penetration of the tumor cells into the tissue and correlates with the Clark scale of description of tissue involvement.¹

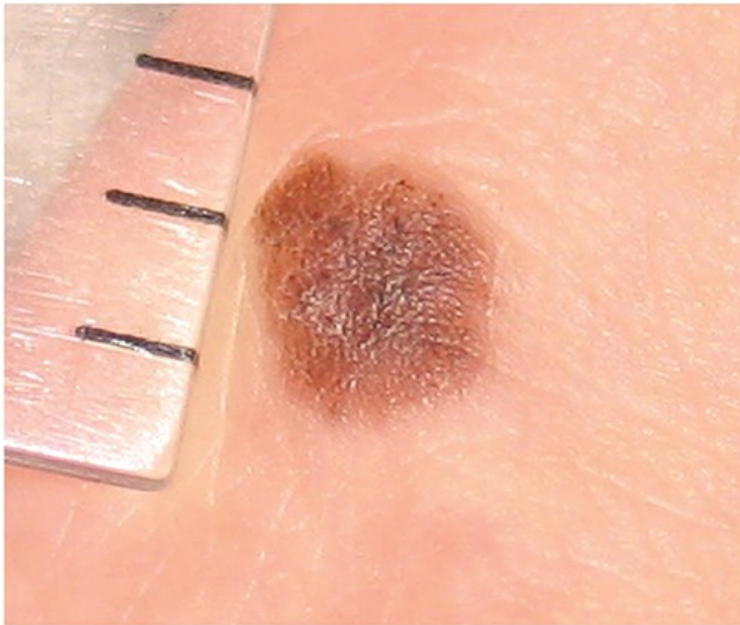
Clinical Presentation

Melanomas are best described by the ABCDE presentation (**FIGURE 8-32**).

- Asymmetry of the discolored area
- Borders that are uneven and distinct
- Color that is dark brown or black
- Diameter more than 1 cm
- Evolution to larger, darker lesion

FIGURE 8-32

Melanoma Melanoma is diagnosed by asymmetry, uneven borders, dark brown or black color, diameter greater than 1 cm, and visible changes in the appearance. Early excision is necessary to prevent metastasis.



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Medical Management

The first treatment of melanoma is excision and afterwards, depending on the depth of tissue involved, chemotherapy and radiation may be necessary.^{102,103}

Wound Management

Wound care is not indicated unless there is failure of the incisional wound to heal.

Kaposi Sarcoma

Pathophysiology

Kaposi sarcoma (KS) is a malignant tumor of the lymphocytic and endothelial cells linked to the herpetic viruses and HIV (FIGURE 8-33). The pathogenesis of KS has now been identified as the human herpes virus type 8.¹⁰⁴ Four clinical variants have been identified:

- Localized, slowly progressing form in older men (classic KS)

- Endemic African KS
- Immunosuppressive KS, usually associated with organ transplant recipients
- Rapidly progressive form associated with HIV or AIDS¹⁰⁵

FIGURE 8-33

Kaposi sarcoma Kaposi sarcoma is most frequently associated with HIV/AIDS, although it can occur in other immunosuppressed individuals. It is slow growing and treatable with excision and radiation. (Used with permission from Tschachler E. Kaposi's sarcoma and angiosarcoma. In: Goldsmith LA, Katz SI, Gilchrist BA, Paller AS, Leffell DJ, Wolff K. eds. *Fitzpatrick's Dermatology in General Medicine*. 8th ed. New York, NY: McGraw-Hill; 2012:chap. 128. Available at: <https://accessmedicine-mhmedical-com.ezproxy.cihe.edu.hk/content.aspx?bookid=392§ionid=41138847>. Accessed January 10, 2019.)



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Clinical Presentation

KS lesions can appear anywhere on the body, including the mucous membranes. The lesions are slightly raised, elongated with poorly demarcated edges, and may have rust or purple-red maculae or patches. They progress slowly into firm necrotic plaques with underlying nodules.¹⁰⁵ Marked edema may develop when the tumors involve the lymphatic vessels, leading to diffuse edema and subsequent skin breakdown.

Differential Diagnosis

- Diabetic wounds
- Venous wounds
- Pyogenic granuloma
- Squamous cell carcinoma

- Melanoma

Medical Management

KS associated with AIDS is treated with highly active antiretroviral therapy (HAART). Surgical excision, local radiation therapy, and cryotherapy are used for isolated cutaneous lesions. For immunosuppressed patients, rapamycin or reduction of immunosuppressive therapy is recommended.¹⁰⁵

Wound Management

Immediate treatment of KS may include topical application of 9-*cis*-retinoic acid ([alitretinoin gel](#)), which has been proven superior to previously used vehicle gel.^{104,106}

Because of the radiation, lymphatic involvement, and edema, chronic wounds may develop (especially if the lesion is on the lower extremity) even years after the tumor has been eliminated. Standard wound care using the TIMEO₂ principles and compression therapy is recommended, and adjunctive therapies such as HBOT and electrical stimulation may be beneficial *if* there are no signs of malignant cells.

Merkel Cell Carcinoma

Pathophysiology

Merkel cell carcinoma (MCC), involving the Merkel cells in the epidermis, is a skin cancer associated with UV exposure that tends to occur in older individuals who are also immunosuppressed. It has recently been shown to contain a polyomavirus. MCC can progress rapidly into the lymph nodes; therefore, it needs early diagnosis and interventions.

Clinical Presentation

Initial MCC presentation is much like a cyst, often resulting in misdiagnosis ([FIGURE 8-34](#)). MCC can be identified using the acronym AEIOU as defined in [TABLE 8-14](#) and if three of the five characteristics are present, there is a high probability of MCC and a biopsy is recommended.¹⁰⁷

FIGURE 8-34

Merkel cell carcinoma Merkel cell carcinoma on the elbow of an 85-year-old lady. She had four of the five characteristics of MCC and was treated with surgical excision.



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TABLE 8-14

Signs and Symptoms of Merkel Cell Carcinoma

| |
|--|
| Asymptomatic (nontender, firm, red, purple, or skin-colored papule or nodule; ulceration is rare) |
| Expanding rapidly (significant growth noted within 1–3 months of diagnosis, but most lesions are <2 cm at time of diagnosis) |
| Immune suppression (eg, HIV/AIDS, chronic lymphocytic leukemia, solid organ transplant) |
| Older than 50 years |
| Ultraviolet-exposed site on a person with fair skin (most likely presentation, but can also occur in sun-protected areas) |

A lesion with three or more of these signs should be biopsied to rule out Merkel cell carcinoma.

Medical Management

Medical management begins with surgical excision, preferably with Mohs technique, followed by radiation and chemotherapy (especially for palliative care of advanced disease or for patients who cannot undergo surgery).¹⁰⁷

Wound Management

Prior to surgery, exudate can be managed with absorbent dressings. After surgery, any excision wounds can be managed with standard wound care.

Cutaneous Lymphoma

Pathophysiology

Although lymphomas generally originate in the lymph nodes or in collections of lymphatic tissue in organs, such as stomach or intestines, the skin may also be affected. Cutaneous lymphomas represent clonal proliferation of neoplastic B cells or T cells that migrate to the skin and cause progressive lesions. **TABLE 8-15** presents a list of primary cutaneous lymphomas, the most common being mycosis fungoides (**FIGURE 8-35**).¹⁰⁸

FIGURE 8-35

Cutaneous lymphoma Mycosis fungoides have three stages: patches, plaques, and nodules as seen in the lower extremity of this patient with systemic metastasis as well as diffuse ulcerated lesions. Patients who have progressed to this stage have a poor prognosis.



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TABLE 8-15

Classification of Primary Cutaneous Lymphoma (WHO-EROTC)

| Cutaneous T-Cell and NK-Cell Lymphomas |
|--|
| <ul style="list-style-type: none"> • Mycosis fungoides |
| <ul style="list-style-type: none"> • Mycosis fungoides variants and subtypes <ul style="list-style-type: none"> ◦ Folliculotropic mycosis fungoides ◦ Pagetoid reticulosis ◦ Granulomatous slack skin |
| <ul style="list-style-type: none"> • Sézary syndrome |
| <ul style="list-style-type: none"> • Adult T-cell leukemia/lymphoma |
| <ul style="list-style-type: none"> • Primary cutaneous CD30-positive lymphoproliferative disorders <ul style="list-style-type: none"> ◦ Primary cutaneous anaplastic large-cell lymphoma ◦ Lymphomatoid papulosis |
| <ul style="list-style-type: none"> • Subcutaneous panniculitis-like T-cell lymphoma |
| <ul style="list-style-type: none"> • Extranodal NK/T-cell lymphoma, nasal type |
| <ul style="list-style-type: none"> • Primary cutaneous peripheral T-cell lymphoma, unspecified <ul style="list-style-type: none"> ◦ Primary cutaneous aggressive epidermotropic CD8⁺ T-cell lymphoma (provisional) ◦ Cutaneous γ/δ T-cell lymphoma (provisional) ◦ Primary cutaneous CD4⁺ small- or medium-sized pleomorphic T-cell lymphoma (provisional) |
| <ul style="list-style-type: none"> • Cutaneous B-cell lymphomas <ul style="list-style-type: none"> ◦ Primary cutaneous marginal zone B-cell lymphoma ◦ Primary cutaneous follicle center lymphoma ◦ Primary cutaneous diffuse large B-cell lymphoma, leg type ◦ Primary cutaneous diffuse large B-cell lymphoma, other ◦ Intravascular large B-cell lymphoma (provisional) ◦ Precursor hematologic neoplasm ◦ CD4⁺/CD56⁺ hematodermic neoplasm (blastic NK-cell lymphoma) |

Used with permission from Beyer M, Sterry W. Cutaneous lymphoma. In: Goldsmith LA, Katz SI, Gilchrist BA, Paller AS, Leffell DJ, Wolff K, eds. *Fitzpatrick's Dermatology in General Medicine*. 8th ed. New York, NY: McGraw-Hill; 2012:chap. 145. Available at: <https://accessmedicine-mhmedical-com.ezproxy.cihe.edu.hk/content.aspx?bookid=392§ionid=41138867>. Accessed January 10, 2019.

Clinical Presentation

Cutaneous lymphoma may present as various types of skin lesions, but rarely as an open wound. Mycosis fungoides begin as patches of scaly erythema and progress to plaques of sharply demarcated, scaly, elevated lesions that are dusky red to violet. The next, most severe stage is nodular in which the malignant cells cause formation of reddish-brown or purplish-red and smooth-surfaced nodules, which often ulcerate and often become secondarily infected.¹⁰⁸ Ulcerative cutaneous lymphomas are associated with poor prognosis; they are increasingly observed in severely immune-compromised patients.

Differential Diagnosis

- Dermatitis
- Vascular wounds
- Eczema
- Psoriasis

Medical Management

Spot radiotherapy is used to treat isolated cutaneous lesions; topical chemotherapy can be useful for patches and plaques. Chemotherapy in conjunction with immunotherapy is used for progressive, diffuse lesions or systemic disease. Psoralen+UVA (PUVA) phototherapy is used for long-term maintenance therapy of patches and plaques.¹⁰⁹ A combination of interferon alpha 2b and low doses of [methotrexate](#) was shown to have good survival rate and minimal toxicity in a study done on patients with relapsed cutaneous T-cell lymphoma by Aviles et al.¹¹⁰

Wound Management

Supportive wound care is indicated for any nonhealing ulcerated lesions.

MISCELLANEOUS

Spider Bites

Pathophysiology

More than 50 spider species in the United States have been implicated in causing significant medical conditions; however, there are two main species that are most known for causing skin necrosis and open wounds: *Loxosceles reclusa* (brown recluse) and *Latrodectus* (black widow). In both cases, the wound severity depends on the venom load and the host immune response. The venom responsible for skin necrosis is a water-soluble substance that contains eight enzymes (including sphingomyelinase D, [hyaluronidase](#), esterase, and alkaline phosphatase) which destroy the tissue they invade, a process termed loxoscelism. Approximately 10% of spider bites progress to necrosis.¹¹¹ The brown recluse is so named because it tends to reside in dark, secluded places such as closets, attics, and woodpiles, and is not aggressive. It bites only when it is disturbed and requires counter pressure to inject the venom.¹¹²

Clinical Presentation

Because most spiders are not seen at the time of the bite (80%), making a definitive diagnosis can be difficult. Only about 12% of the victims are able to bring the spider to the medical facility after the bite. The initial response is minor stinging or burning, followed by development of an erythematous macule surrounding a central papule.¹¹¹ If there is sufficient venom or the host is immunosuppressed, the bite may progress to severe inflammation with a “bull's-eye” appearance, followed by a red, white, and blue discoloration as the lesion enlarges ([FIGURES 8-36](#) and [8-37](#)). If the tissue becomes anoxic, necrosis with an eschar will develop, usually after 72 hours, with underlying fatty necrosis. Viscerocutaneous loxoscelism or systemic signs may include rash, fever, chills, nausea, vomiting, malaise, arthralgia, and myalgia. In severe rare cases, renal failure may occur with hemolysis, hemoglobinuria, leukocytosis, leukopenia, or thrombocytopenia.^{113,114}

FIGURE 8-36

Bull's eye sign of spider bite Within hours after a brown recluse spider bite, there will be a distinctively visible spot where the venom was injected, termed the “bull's eye.” (Used with permission from Zafren K, Thurman R, Jones ID. Environmental conditions. In: Knoop KJ, Stack LB, Storrow AB, Thurman R, eds. *The Atlas of Emergency Medicine*. 3rd ed. New York, NY: McGraw-Hill; 2010:chap. 16.)



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FIGURE 8-37

Red, white, and blue discoloration of spider bite As the venom spreads there is a red, white, and blue discoloration of the affected tissue. At this point, the patient may require surgical excision of the necrotic tissue with wound healing by secondary intention or closure by plastic reconstruction. (Used with permission from Zafren K, Thurman R, Jones ID. Environmental conditions. In: Knoop KJ, Stack LB, Storrow AB, Thurman R, eds. *The Atlas of Emergency Medicine*. 3rd ed. New York, NY: McGraw-Hill; 2010:chap. 16.)



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Differential Diagnosis

- Foreign body reaction
- Infections (mainly MRSA)

- Trauma
- Vasculitis
- Pyoderma gangrenosum
- Squamous cell carcinoma
- Lyme disease

Diagnosis is made by positive identification of the spider, complete blood count if there are systemic effects, urinalysis if there is renal failure, and ELISA (enzyme-linked immunosorbent assay), which can check for the specific antigen.¹¹⁵

Medical Management

Treatment of spider bites may begin with excision of the bite location. [Dapsone](#) administered within 24 hours is advised to inhibit neutrophil migration (except in the case of G6PD deficiency), and systemic steroids may prevent enlargement of the necrotic area. Other medical interventions include oral antihistamines, glucocorticoids, and antivenom. Prophylactic antibiotics are indicated for immunosuppressed victims.

Wound Management

Initial first aid includes cooling the bite site to prevent spreading of the venom. If tissue necrosis occurs, debridement and moist wound principles are indicated. Hyperbaric [oxygen](#) therapy may also be useful, especially if the patient has marginal [oxygen](#) supply due to peripheral arterial disease.¹¹¹

Calciphylaxis

Pathophysiology

Calciphylaxis, also known as calcific uremic arteriolopathy, is a potentially fatal condition characterized clinically by progressive cutaneous necrosis as a result of calcification and thrombosis of the dermal arterioles.¹¹¹ Calciphylaxis is seen in 1% of patients with chronic renal failure and in 4.1% of patients receiving hemodialysis. In addition, it usually occurs in patients with Type 2 diabetes and end-stage renal disease who have been on hemodialysis for more than 10 years.¹¹⁷ Other risk factors for calciphylaxis include female sex, obesity, recurrent hypotension, elevated time-averaged serum phosphorous levels, reduced time-averaged serum [albumin](#) levels, and [warfarin](#) therapy.¹¹⁸ More than 50% of the patients die within 1 year of diagnosis, usually from sepsis.¹¹⁶

The pathogenesis of calciphylaxis is still poorly understood. Patients who are on long-term dialysis usually develop abnormal calcium-phosphorus products, which in turn lead to tertiary hyperparathyroidism. This results in elevated calcium-phosphate products and the development of microvascular calcification that in turn leads to tissue necrosis.¹¹¹ Histology shows calcification of the intima and media of small and medium vessels in the dermis and subcutaneous tissue.^{119,120}

Clinical Presentation

The cutaneous manifestations of calciphylaxis begin as sudden-appearing red or violaceous mottled plaques in a livedo reticularis pattern. The early ischemic lesions often progress to gangrenous, poorly defined, black plaques and/or nodules. With time, the plaques ulcerate and become exquisitely tender. Usually ulcers are on the lower extremities, bilateral, symmetric, and may extend deep into muscle (**FIGURES 8-38 and 8-39**).

FIGURE 8-38

Calciphylaxis, early onset Early onset of calciphylaxis appears as erythema and ischemia with severe anoxic pain.



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FIGURE 8-39

Calciphylaxis, progression of skin lesion As the disease progresses, the skin necrosis becomes more extensive and more painful; the patient is at higher risk for mortality.



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Differential Diagnosis

- Pyoderma gangrenosum
- Coumadin-induced skin necrosis
- Necrotizing fasciitis
- Pressure-induced tissue loss

Medical Management

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Chapter 8: Atypical Wounds, Rose L. Hamm; Jayesh B. Shah

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Multiple approaches to medical management of calciphylaxis are recommended to prevent infection, manage pain, and optimize outcomes by chelating arterial calcium. Treatment strategies include the following:

- Systemic antibiotics
- Opioid pain medication ([morphine](#) can cause hypotension and slow blood flow in the arterioles, as well as diminished appetite that can lead to malnutrition and impaired wound healing)
- Phosphate binders such as [sevelamer](#)
- Sodium thiosulfate as a chelating agent for calcium deposits in the tissue
- Bisphosphonate therapy to help remove arterial calcification
- Low calcium hemodialysis for patients with ESRD
- [Cinacalcet](#) to lower parathyroid levels and improve calcium-phosphorus homeostasis
- Hyperbaric [oxygen](#) therapy to increase local tissue [oxygen](#) perfusion
- Low calcium diet to optimize nutrition and provide adequate calorie and protein intake for wound healing^{116,121,122}

In the past, parathyroidectomy was performed in an effort to increase calcium uptake; however, this procedure has not been shown to be significantly effective and is reserved for patients with known hyperparathyroidism.¹²³ Also, systemic corticosteroids are not recommended as they may exacerbate arteriolar calcification.

Wound Management

Debridement of necrotic tissue and calcified vessels is needed for reversal of the inflammatory response to calciphylaxis; however, this is difficult to perform bedside if the necrosis is extensive because of the intense pain levels associated with the disease. Surgical debridement followed by negative pressure wound therapy is the most expeditious approach if the patient is medically stable for surgery. This is complemented by skin grafting with either autologous or tissue-engineered skin, or use of a dermal replacement matrix.¹²³ Intralesional sodium thiosulfate (250 mg/mL) injected or instilled into areas of clinically active disease has been shown to reduce pain and resolve the purpura of calciphylaxis lesions, and [pentoxifylline](#) can facilitate vasodilation.¹²² Electrical stimulation and hyperbaric [oxygen](#) therapy may be beneficial adjunct therapies. In addition to the meticulous wound care (using aseptic technique to prevent infection), nutritional supplements and monitoring are advised because patients may have difficulty eating sufficient calories for wound healing given the amount of pain medicine required to manage the anoxic pain.

Coumadin-Induced Skin Necrosis

Pathophysiology

Coumadin-induced skin necrosis is a rare complication of anticoagulation therapy in individuals who have a thrombophilic history or after administration of a large dose of Coumadin (also [warfarin](#)), particularly without simultaneous initial use of heparin.¹²⁴ Although the exact pathogenesis is unknown, it is understood that protein C deficiency, protein S deficiency, Factor V Leiden, hyperhomocysteinemia, antiphospholipid antibodies, and [antithrombin](#) III deficiency are common underlying factors. Symptoms usually begin between the 3rd and 10th days after starting anticoagulation therapy.¹²⁵ Sometimes postpartum women have reduced levels of free protein S during antepartum and immediate postpartum periods.¹²⁶

Clinical Presentation

Skin changes usually appear on the breasts, buttocks, abdomen, thighs, and calves, probably due to the reduced blood supply to adipose tissue.¹²⁴ Initial symptoms include patient complaints of paresthesias, sensations of pressure, and exquisite pain, followed by presentation of erythematous

flush that becomes edema with *peau d'orange* appearance. Within 24–48 hours, petechiae and purpura appear and become hemorrhagic bullae that progress to hemorrhagic necrosis (**FIGURE 8-40**).¹²⁷

FIGURE 8-40

Coumadin-induced skin necrosis Coumadin-induced skin necrosis usually develops days after beginning the medication. Treatment involves first stopping the medication, debridement of the necrotic tissue, and moist wound care.



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Differential Diagnosis

- Necrotizing fasciitis
- Gangrene
- Calciphylaxis
- Pyoderma gangrenosum
- Purpura fulminans
- Cryofibrinogenemia
- Disseminated intravascular coagulation
- Cellulitis

Medical Management

The most important aspect of treatment is discontinuation of the anticoagulant, along with pain management and infection prevention. IV [heparin](#) or low-molecular weight [heparin](#) may be substituted for Coumadin,¹²⁴ and fresh frozen plasma and subcutaneous vitamin K are used to reverse the Coumadin effect quickly.¹²⁷

Wound Management

Wound management includes debridement (surgical, sharp, or autolytic, depending on the depth and amount of necrotic tissue), moist wound therapy, skin grafts, and/or bioengineered skin. If surgical debridement involves loss of subcutaneous tissue, negative pressure wound therapy may assist in wound bed preparation for surgical closure.

Sickle Cell Wounds

Pathophysiology

Sickle cell ulcers are a complication of sickle cell anemia, an inherited genetic disorder in which the red blood cells have a sickle shape, rendering them incapable of binding hemoglobin. This leads to hypoxia that can cause severe pain crises and can also deprive injured tissue of the [oxygen](#) necessary for healing. The patient with the homozygous form of sickle cell disease is most likely to develop a sickle cell ulcer. Studies have shown that males are more likely than females to develop leg ulcers due to sickle cell disease.¹²⁸

In sickle cell disease, the abnormal hemoglobin molecule in the red blood cell causes a change in the shape of the RBC. In addition, when cells are in the sickled shape, they tend to increase blood viscosity. This causes slowing of the blood flow in small vessels, which also contributes to ischemia of tissue and organs. Over time, the patient suffers repeated episodes of pain, tissue damage, and eventually, organ failure. Although the exact cause of sickle cell ulcers is not clear, they have been associated with trauma, infection, severe anemia, warm temperatures, and venous insufficiency.¹²⁹

Clinical Presentation

Sickle cell ulcers are found on the lower third of the leg, usually over the medial and/or lateral malleoli of the ankle ([FIGURE 8-41](#)). They are exquisitely painful and can have a thick layer of fibrinous tissue, slough, or biofilm. The edges tend to be even like an arterial wound, and the wound bed is slow to granulate. Because of the chronic inflammatory state and reduced ankle function due to pain, lower extremity edema may be present and thus complicate the healing process.

FIGURE 8-41

Sickle cell wound The patient with sickle cell disease may develop a spontaneous ulcer or may have difficulty healing a wound that has another etiology. This patient had a chemical burn on the lower leg that became chronic and was debilitating because of the pain, drainage, and resultant loss of ankle function. He was treated medically with transfusions and [deferasirox](#) to chelate the iron; locally, with nonadherent antimicrobial dressings, compression therapy, exercise to increase the ankle range of motion and strength of the venous pump, and gait training. He healed fully and was able to return to work.



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Differential Diagnosis

- Venous insufficiency ulcers

- Vasculitis

Medical Management

Treating patients who have wounds and sickle cell anemia requires a combination of therapies in order to optimize healing. Medical management of the sickle cell disorder includes oral zinc sulfate (200 mg three times per day)¹³⁰ and a combination of l-methylfolate calcium, pyridoxal-5 phosphate, and methylcobalamin (Metanx). The goal is to decrease endothelial cell homocysteine levels and raise nitric oxide levels, resulting in improved wound healing. It also helps reduce pain associated with sickle cell ulcers and increase blood flow in the microcirculation at the wound margin.^{131,132}

Transfusion therapy is advised with a goal of keeping the hematocrit level between 30 and 35 and the level of normal hemoglobin (hemoglobin A) greater than 70% of the total. The transfusions are continued until the ulcers heals or for 6 months at which time they are discontinued.¹²⁸ In conjunction with transfusions, [deferasirox](#) is administered to chelate the excess iron that accumulates with transfusions.¹³³

IV [arginine](#) butyrate can also help change the concentration of abnormal hemoglobin, thus facilitating wound healing.¹³¹ [Pentoxifylline](#) (Trental) is a vasodilator used to treat peripheral arterial disease that may also help increase the peripheral tissue perfusion.

Wound Management

Basics of good wound care include debridement of devitalized tissue, control of infection, assurance of adequate circulation, and maintenance of a moist wound environment.¹³⁴ Specific strategies that have been included in the literature include the following:¹³⁵

- Negative pressure wound therapy
- Antibiotics
- Biofilm removal
- Compression therapy
- Topical growth factor (granulocyte-macrophage colony-stimulating factor)
- Honey-based dressing
- Bioengineered skin¹³⁶
- Split thickness skin graft
- Hyperbaric [oxygen](#) therapy
- Electrical stimulation or electromagnetic therapy

Factitious Wounds

Pathophysiology

Patients with factitious disorder (FD) use false symptoms or self-injury in order to appear sick and/or to gain access to medical care. More than 62% of the patients are female and the mean age is 34.2 years. FD is similar to somatic symptom disorder, another mental disorder that involves the presence of skin lesions that are not due to actual physical illnesses. Rather the wounds are deliberately and consciously self-inflicted and not allowed to heal because of patient interference with care.^{1,19}

Clinical Presentation

Factitious wounds usually have geometric edges and healthy granulation tissue, and are located on areas of the body that are easily accessible with the

hands (eg, face, arms, torso, legs, but rarely on the back) (FIGURE 8-42). Of most importance is the patient denial of any responsibility for the wound and lying about compliance with care.¹³⁷

FIGURE 8-42

Factitious wounds When wounds that should heal with standard care fail to do so, factitious behavior is a consideration. Suspicious signs are failure to retain dressings between treatments, evidence of “picking” at the wound, or waxing and waning of wound progression. This patient who had extensive wounds on the upper extremities from vein popping drugs exhibited factitious behavior after being released from the hospital. She was inconsistent in keeping appointments, arrived without dressings, and had the typical granulated wound base with geometric edges.



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Differential Diagnosis

Once the clinician is suspicious that a nonhealing wound is the result of self-inflicted behavior, differential diagnosis of factitious wounds is dependent on diagnosis of an underlying psychological or psychiatric disorder (eg, delusional disorder, depression, anxiety, emotional deprivation, personality disorder with borderline features, schizophrenia).

Medical Management

Medical management includes treatment of the underlying psychiatric disorder, any comorbidities, and other complications that may arise from the induced illness.¹³⁸

Wound Management

Standard wound care with occlusive dressings, avoidance of invasive procedures, supportive emotional care, thorough documentation, and close observation are required for the clinician caring for a patient with factitious wounds.¹³⁸ Adherence to treatment strategies will need continuous reinforcement for both the patient and family/care givers.

SUMMARY

When wounds have an unusual appearance or fail to respond to standard care, further evaluation is required to determine the diagnosis of what is termed atypical wounds. Signs of atypical wounds include unusual location, unusual age, poor or friable granulation tissue, overgrowth, red or purple periwound skin, or history of diseases that suggest other wound diagnoses. Atypical wounds can be generally categorized into allergic reactions, infections (viral, bacterial, or fungal), autoimmune disorders, malignancies, or factitious behavior. Successful treatment of the wound is predicated on

making the correct diagnosis of underlying diseases as well as the wound or integumentary disorder. Referral to the appropriate medical specialist is also an integral part of caring for the patient with an atypical wound.

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